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Research: a teaching aid in graduate programs

■ *Morgan L. Allison,* D.D.S., Columbus, Ohio*

This is a welcome opportunity to present the purpose and methods of investigational studies incorporated in a graduate training program in oral surgery. Academic courses are correlated with clinical training during the three year program at Ohio State University. Research is arranged to complement both the academic and clinical training. Overlap between them is desirable and should not detract from fulfilling the purposes of the program.

Areas of research may be clinical, laboratory or literature investigations. Clinical studies may be controlled with double blind technics or careful, unbiased observations. Laboratory investigations lend themselves to more accurate controls and wider range of materials and methods. Experience in research in the literature trains the student to interpret data critically and to establish general patterns. These areas of research are limited by the purpose of the investigation, the qualifications of the investigator and the facilities available. Explorations of such nature should be used to teach students to solve problems scientifically.

Facilities for research are the responsibility of the chief of service. Grants should be obtained to finance research. Interdepartmental use of laboratories reduces costs and increases efficiency. Interdepartmental cooperation and advice leads to better understanding of and respect for dentistry by allied health groups. Careful guidance of the graduate student by his adviser is necessary in setting up and solving the problem; in interpreting and publishing the results. However, the student must be encouraged to express his own opinions of results and conclusions.

"Why don't we do more research in oral surgery or anesthesia?" is a question asked frequently. "Why do we devote so much effort to these laboratory and animal studies? Can't we investigate strictly oral surgery or anesthesia questi ns?" Actually, disciplines learned during training help the student evaluate results of basic science research and select possible practical applications from these results.

Technical advances are achieved by application of research results. Dentistry must continue to accept the obligation of developing areas of research to maintain the standard of practice the profession expects. Privileges in the overlapping areas

between dentistry and other health professions depend to a large degree on the acceptance of dentistry in these areas. No better evidence than the results of good research is available to dentistry to facilitate this acceptance.

An important part of graduate education is to learn good journalism. Practical application of journalism is made by writing term papers, case reports and the thesis. Close supervision of student writing for publication is essential. Under ordinary circumstances graduate students or residents do not have sufficient experience and are not sufficiently authoritative to write comprehensive research reports or reports of difficult or controversial operative procedures. Exceptions to these rules are those papers carefully reviewed and edited by the faculty adviser for the student. With these points in mind, the scope of papers in this issue can be examined.

The case reports are limited to one aspect of operative procedures in our program. Limitations of time and space preclude additional material. The case reports represent an example of review of the literature. The graduate student house staff served as first assistants on each of these cases. The case history, histopathologic specimen and general review of the pathology were reviewed and written by the house staff author. The case reports were then edited by the operating oral surgeon and the staff oral pathologist. This authority is lent to presentation of these cases.

The papers in this issue present a wide range of subjects and great variation in the complexity of the investigation, depending on the purpose of the assignment. It must be emphasized that such investigational projects must not detract from clinical training. Although these projects lead to discovery of new scientific knowledge, they should be designed also to teach the student to solve problems scientifically. Reports such as these teach the student principles of journalism and enable him to make future contributions to the literature of oral surgery.

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The effect of surgery on blood coagulation

■ *Walter C. Maslowski,* D.D.S., Columbus, Ohio*

Investigation by serial laboratory tests preoperatively and postoperatively demonstrates that surgery alters the coagulability of the blood. More severe surgical procedures produce a tendency to increased coagulability and less severe procedures to decreased coagulability. A recently developed test, the fibrinogen conversion index, was used to follow these changes in 11 patients. Plasma fibrinogen and thromboplastic plasma component concentrations showed consistent elevation after surgery regardless of its severity.

Do changes occur in the coagulability of blood after a person is injured?

Investigators have used available tests carefully and have tried to answer this question.[1-18] Most of these tests were qualitative or clotting time studies. The tests considered only one phase or one component of the clotting mechanism. Results were inconsistent and difficult to reproduce.

In 1957 Shinowara[19] reported the results obtained in a study of coagulation components during the spontaneous clotting of blood. His experiments indicated that coagulation components are depleted in a definite sequence. Activators of prothrombin, platelets and thromboplastic plasma component (antihemophilic globulin) were expended first. Fibrinogen and prothrombin were depleted next. Antithrombin globulin activity never fell below 54 per cent of the original value. These results definitely indicate that fibrinogen occupies an intermediate position in the utilization of certain important coagulation factors during the clotting process. On the basis of these findings, a critical quantitative method for measuring blood coagulability, the fibrinogen conversion index, was developed.[20] Shinowara and Hicks measured the fibrinogen remaining at specific intervals in samples of spontaneously clotting blood. They found that this method, actually a measure of the net effect of all known and unknown blood factors, was an accurate way to study coagulation rate.

The fibrinogen conversion index was used in this study to answer three questions:

1. Do changes occur in the clotting mechanism after surgery?
2. When do these changes occur?
3. What causes these changes?

■ *Methods and Materials*

Eleven patients in University Hospital, Ohio State University Health Center, who required oral or orthopedic surgery, were selected. General anesthetics were administered to all patients (thiopental sodium, curare-type

drug, nitrous oxide and oxygen). Preoperative and serial postoperative (1, 3, 7, 10, 15 days) fibrinogen conversion index samples were drawn. A slight modification of the original technic[20] was used to obtain 66 fibrinogen conversion indexes involving 330 duplicate determinations. The duplicated determinations showed a small (±4 per cent) margin of error.

COLLECTION OF BLOOD SAMPLE—The following are prepared:

Four 10 x 100 mm. saline rinsed test tubes. These are marked for 1.8 ml. volume. The tubes are labeled 10, 20, 30 or 40.

One 15 ml. graduated centrifuge tube. In instances where platelet samples are desired, this tube is siliconized.

Two 10 x 100 mm. saline rinsed test tubes. These are marked for 1.0 ml. volume. The tubes are labeled "L-W."

Four 0.2 ml. pipets. These are prepared from 1.0 ml. pipets. Notches are filed at the 0.22 mark. The pipet is broken carefully at this mark. A file and emery paper are used to flatten the cut end back to the 0.2 mark. This pipet now serves to measure citrate and as a plunger.

One stop watch.

One 20 ml. syringe containing 1.5 ml. of 4 per cent sodium citrate. When platelet samples are desired, this syringe is siliconized.

One 10 ml. saline rinsed syringe.

Three sharp, short bevel 20 gauge needles.

One cup of ice water.

The 20 ml. syringe and 20 gauge needle are used to draw blood to the 15 ml. mark. The 20 ml. syringe is detached and is replaced with the 10 ml. syringe. (A nurse or orderly should mix the 15 ml. sample, put it into the centrifuge tube and place the tube in the ice water bath.) Blood is drawn into the 10 ml. syringe. The stop watch is started when the 5 ml. mark is reached. The tourniquet, needle and syringe are removed from the patient's arm when 10 ml. of blood has been drawn. The 10 ml. of blood is portioned into the marked "L-W" 10, 20, 30 and 40 minute tubes. If a poor venipuncture has been made or if trouble is encountered while drawing either sample, no more blood should be drawn from that spot. Poor venipunctures will cause false results. The venipuncture is repeated at another site using clean apparatus.

DETERMINATION OF WHOLE BLOOD CLOTTING TIME (Modified Lee-White)[21]—Three minutes after the stop watch has been started one of the "L-W" tubes is tipped from the vertical to the horizontal plane. This procedure is repeated every 30 seconds until the blood does not flow and its meniscus keeps its contour. This is the end point. The time is recorded. The second tube is tipped like the first and its end point recorded. The time of both tubes is averaged for the whole blood clotting time.

PREPARATION OF 10, 20, 30 AND 40 MINUTE SAMPLES—Ten minutes after the start of the stop watch, 0.2 ml. of 4 per cent sodium citrate is added to the 10 minute tube with the special pipet. The pipet is plunged to the bottom of the tube 15 times to mix the citrate with the blood. This stops clotting in that tube. Exactly 10 minutes after citrate has been added, formed clumps are crushed with the pipet. The pipet is removed and the tube placed in the ice water bath. At the proper time the 20, 30 and 40 minute samples are treated in the same manner as the ten minute sample. Immediately after the 40 minute sample has been mixed, these four tubes are centrifuged at 1,650 times gravity for 15 minutes at 0°C. An International refrigerated centrifuge, model PR-1, was used for all 0°C. centrifugation. With dry bulb pipets the plasma or serum or both are transferred from the spun tubes to labeled dry test tubes.

PREPARATION OF ZERO TIME AND FRACTIONATION SAMPLE—The centrifuge tube is spun at 1,650 times gravity for 30 minutes at 0°C. The plasma is removed with a dry bulb pipet. Four milliliters is put into a fractionation tube, corked, labeled and stored in a freezer at −25°C. for future study. The remaining plasma is used for a zero time sample.

From this point, the 0, 10, 20, 30 and 40 minute samples are treated in the same fashion. A 0.2 ml. sample is placed in each of three

10 x 100 mm. test tubes. A 0.6 ml. citrate phosphate buffer (pH 7.3, R/2, 0.166) is added. These diluted specimens are corked, labeled and stored in a freezer at −25°C. if the analysis is to be postponed.

FIBRINOGEN DETERMINATION—Two specimens of each time sample are used. One of each is saved for recheck studies.

The tubes are placed in a 37°C. water bath and 0.2 ml. bovine thrombin[22,23] (5 NIH units per milliliter) added. The specimens are mixed and the time of clot formation recorded. They are then incubated for 15 minutes.

The clot is loosened by tapping the tube, then is wound around the roughened end of a 4 x 160 mm. glass rod. A different rod is used for each sample. The clot is compressed against the side of the tube and 4 ml. citrate phosphate buffer added. The clot is loosened from the rod and mixed in the buffer solution. Then the clot is squeezed again. The material from the lower half of the rod is washed into the tube with 2.0 ml. of buffer. The rods are placed, roughened end up, in consecutive order in a numbered rack. The sample is centrifuged at 1,650 times gravity at room temperature for 15 minutes, then the supernatant is decanted off carefully. An International centrifuge, size 1, model SBV, was used for room temperature centrifugation.

After completing this procedure, the tube containing the clot is inverted and allowed to drain for 10 minutes. The upper half of the tube is dried with clean gauze, the glass rods replaced in their respective tubes, 2.0 ml. of 2.0 N sodium hydroxide added, then is stirred and put into 37°C. water bath for 15 minutes. Stirring is done every two minutes.

TYROSINE DETERMINATION[24]—One milliliter of sodium hydroxide dissolved protein is put into a 19 mm. cuvette; 4.0 ml. double distilled water and 5.0 ml. dilute Folin-Ciocalteu reagent[25,26] are added. The solution is swirled five or six times. In exactly five minutes the optical density of the solution is determined on a Coleman Junior Spectrophotometer set at 650 millimicrons. A cuvette containing 1.0 ml. of 2.0 N sodium hydroxide, 4.0 ml. of double distilled water and 5.0 ml. of dilute Folin-Ciocalteu reagent is used as a reference blank. The optical density is converted to micrograms of tyrosine using the standard table for chemically pure tyrosine.[25]

CALCULATION OF FIBRINOGEN CONCENTRATION—The fibrinogen content of the test solution is calculated from the following equation:

$$(T - t) \times \frac{100 \text{ ml.}}{0.1 \text{ ml.}} \times \frac{11}{1{,}000{,}000} \times = \text{Gm./100 ml.}$$

T = micrograms tyrosine in test solution.

t = micrograms tyrosine in 0.1 ml. of centrifuged and washed thrombin reagent. "t" in this system is 1.3.

0.1 ml. = the volume of sample dissolved in 1 ml. of sodium hydroxide solution.

11 = the chromogenic factor. This factor represents the micrograms of fibrin solution necessary to equal the reaction of one microgram of pure tyrosine with Folin-Ciocalteu reagent.[20,24,26-30]

C = citrate dilution factor of the original sample. C in this system is 1.17.

Therefore, the foregoing equation can be further simplified (T − 1.3 × 0.011 × 1.17 = Gm. fibrinogen/100 ml. plasma)

CALCULATION OF PER CENT FIBRINOGEN REMAINING—The per cent of fibrinogen remaining is calculated as follows:

$$\text{Per cent fibrinogen remaining} = \frac{D^n}{D^o} \times 100$$

D^n = optical density of zero time sample.

CALCULATION OF FIBRINOGEN CONVERSION INDEX—The percentage of fibrinogen remaining in the 10, 20, 30 and 40 minute samples is totaled to get the fibrinogen conversion index. Theoretically, the index has a range of 0 to 400. A zero index would mean that complete coagulation occurred within ten minutes. Therefore, no fibrinogen remained in any of the samples. A 400 index would mean that no coagulation occurred even after 40 minutes;

that is, all of the fibrinogen remained in all of the samples. A normal, healthy individual has an average index of 149 with a range of 109-216. Hypocoagulable patients, such as hemophiliacs, have a mean index of 266 with a range of 172-396. Hypercoagulable patients, such as those with thrombosis, have a mean index of 71 with a range of 17-111.[20]

In addition to the fibrinogen conversion index, whole blood clotting time, and measurement of fibrinogen, other laboratory studies were carried on. Modified Quick one-stage prothrombin tests[31] were performed on all patients. Platelet counts were done on seven patients picked at random.

For each of eight patients, fractionations[22, 24] were done on preoperative and 1, 3, 7, 10 and 15 day postoperative plasma samples. By fractionation the individual coagulation components can be removed from plasma. In this study prothrombin,[22] thromboplastic plasma component[32] and antithrombin globulin[33] were isolated from each sample. The amounts of these substances were measured.

■ *Results*

For each of 11 patients undergoing oral or orthopedic surgery, fibrinogen conversion index determinations were done. Preoperative samples were drawn 1 to 2 days before surgery and postoperative samples were drawn 1, 3, 7, 10 and 15 days after surgery. In all 66 indexes involving 330 duplicate determinations were obtained in this study. All patients had normal preoperative indexes (120-190). After surgery, the fibrinogen conversion index changed in all patients. Patients could be divided into two groups on the basis of the change in index. One group showed a decrease in fibrinogen conversion index (tendency to increased coagulability). This shall be called the "fast" group. The other group showed an increase in fibrinogen conversion index (tendency to decreased coagulability). This shall be called the "slow" group. Both groups showed a peak index change three days postoperatively. However, the "slow" group returned to the preoperative level much more quickly than the "fast" group (Fig. 1). Eight of the 11 patients were in the "fast" group. Two of the eight showed decreased coagulability at one day but subsequently showed the typical tendency to increased coagulability. All five orthopedic patients and three oral surgery patients were in the "fast" group.

Clinical data were compiled on all patients and correlated with changes in the fibrinogen conversion index. It was found that the amount of surgical trauma was most important in altering coagulability. Criteria used to evaluate the amount of trauma included: amount of blood loss, duration of surgery, size and location of the area of surgery, variations in postoperative temperature and length of the postsurgical convalescent period. When surgery was more severe, there was a tendency to increased coagulability of blood. When surgery was less severe, there was a tendency to decreased coagulability. It was also noted that patients with a "fast" response had preoperative white blood cell counts of 8,200 to 13,500; those with a "slow" response, 4,650 to 5,400.

Samples for seven other laboratory studies were drawn on the same days that samples for fibrinogen conversion index determinations were collected. Lee-White gross coagulation times and modified Quick one-stage prothrombin determinations done on each patient showed no significant deviations even on the days when the fibrinogen conversion indexes demonstrated peak changes. Forty-two platelet counts were done on seven pa-

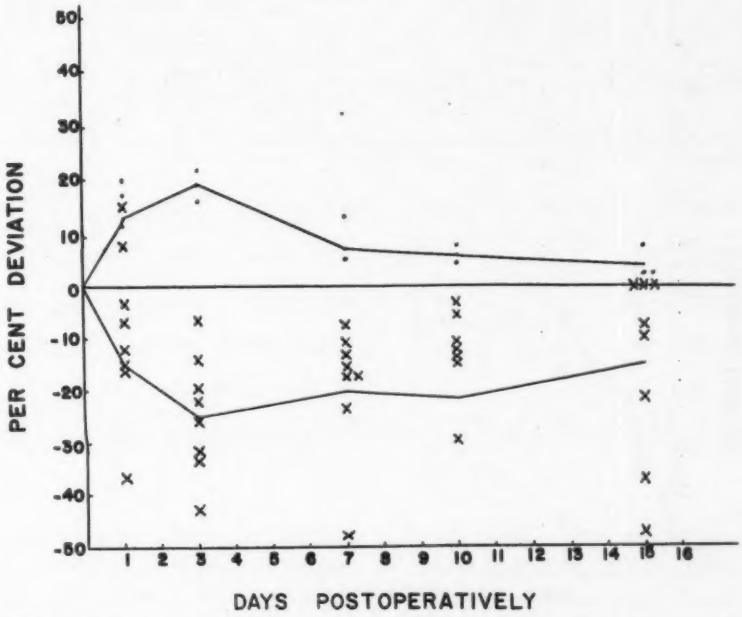

Fig. 1—Per cent of deviations of fibrinogen conversion index after surgery. • = "slow" group; X = "fast" group

tients (five from the "fast" group and two from the "slow" group). Regardless of the group, platelet counts followed the same trend. At three days there was a decrease (18 to 30 per cent below preoperative level). At seven days there was a substantial increase (11 to 18 per cent above preoperative level). At 10 and 15 days there was still an increase (10 to 30 per cent and 2 to 15 per cent above preoperative level).

In respect to the plasma fibrinogen concentration after surgery, one very important observation was made. Plasma fibrinogen concentration showed a definite elevation in 10 of the 11 patients. This elevation occurred irrespective of the fibrinogen conversion index change. The fibrinogen concentration in the "fast" group rose to a peak of 36 per cent above the preoperative level by the third day and was still elevated at the fifteenth postoperative day. The fibrinogen concentration in the "slow" group rose to a peak of 39 per cent by the first day and was still elevated at the fifteenth day also (Fig. 2).

For each of eight patients (six in the "fast" group and two in the "slow" group), fractionations were done on preoperative and 1, 3, 7, 10 and 15 day postoperative plasma samples. By fractionation, individual coagulation components can be removed from plasma. In this study prothrombin, thromboplastic plasma component (antihemophilic globulin) and antithrombin globulin were isolated

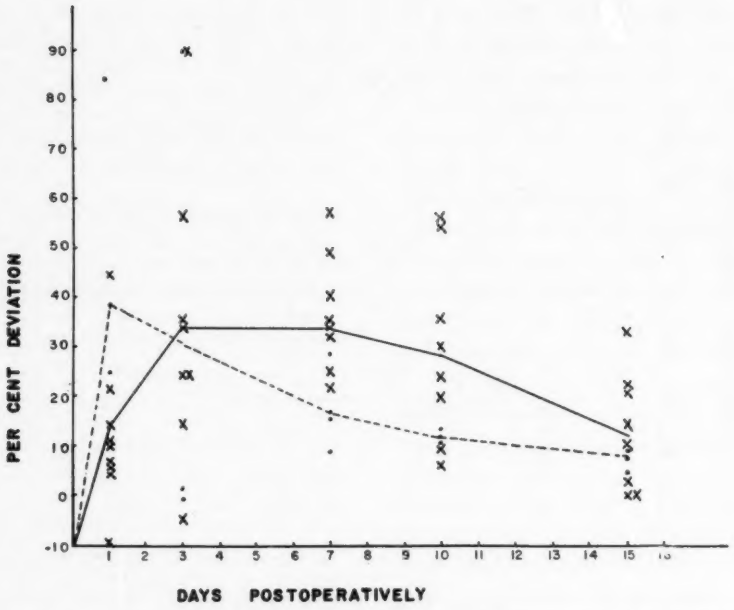

Fig. 2—Per cent of deviations of plasma fibrinogen concentrations after surgery. • and dotted line = "slow" group; X and bold line = "fast" group

from each sample. The amounts of these substances were then measured.

Prothrombin exhibited little deviation (± 7 units per milliliter) from day to day in seven of the eight patients. In the eighth patient, Case 9, who had a postoperative increase in the fibrinogen conversion index, the prothrombin concentration rose from 84.0 units per milliliter preoperatively to 126.0 units per milliliter by the third postoperative day and was still elevated (120 units per milliliter) on the tenth day.

In four of six patients (Cases 1-4) demonstrating definite diminution in the fibrinogen conversion index, postoperative thromboplastic plasma component concentration rose from 3 to 260 per cent whereas antithrombin globulin concentration fluctuated between +46 per cent and −15 per cent. This is demonstrated by Case 1 in Table 1. In one of the six, Case 7, the thromboplastic plasma component concentration rose to 740 per cent above the preoperative level by the third postoperative day and was still elevated (137 per cent) on the fifteenth day. Antithrombin globulin in this patient manifested the same fluctuations as in the other four patients. In the sixth patient, Case 4, the thromboplastic plasma component concentration showed a decrease and antithrombin globulin rose slightly after surgery as shown by the data in Table 2.

Two patients whose fibrinogen conversion index rose after surgery were also

Table 1 • Results of tests in Case 1*

Sample	Fibrinogen (Gm. per 100 ml.)	Thromboplastic component (u/ml.)	Prothrombin (u/ml.)	Antithrombin globulin (u/ml.)	Fibrinogen conversion index	Lee-White clotting time (min.)	Platelets (per cubic mm.)	Hematocrit
Preoperative	.502	179.8	68.0	184.4	163	6.5	172,050	40
1 day postoperative	.531	230.2	67.5	251.1	159	6.0	216,450	43
3 days postoperative	.682	262.7	71.4	262.4	92	6.0	144,300	41
7 days postoperative	.488	174.3	64.0	191.3	84	6.0	227,550	35
10 days postoperative	.616	228.2	66.3	229.9	73	6.5	227,550	36
15 days postoperative	.607	229.1	60.7	183.7	79	6.0	244,200	34

*An arthroplasty of the left hip was performed on this 47 year old white woman. She exhibited the most pronounced and prolonged "fast" response of any patient in the study.

definitely investigated. In Case 10 the fibrinogen index rose to 14 per cent above the preoperative level by the third postoperative day and returned to the preoperative level by the seventh day. In this patient, thromboplastic plasma component concentration showed a slight increase, but there was essentially no change in antithrombin globulin and prothrombin concentrations as can be seen in Table 3. On the other hand, in Case 9, despite a significant rise in the thromboplastic plasma component (152 to 468 per cent) and prothrombin concentrations

Table 2 • Results of tests in Case 4*

Sample	Fibrinogen (Gm. per 100 ml.)	Thromboplastic component (u/ml.)	Prothrombin (u/ml.)	Antithrombin globulin (u/ml.)	Fibrinogen conversion index	Lee-White clotting time (min.)	Platelets (per cubic mm.)	Hematocrit
Preoperative	.386	58.6	80.1	143.9	135	7.0	166,400	41
1 day postoperative	.436	57.4	76.9	151.5	85	7.5	183,150	44
3 days postoperative	.449	57.9	75.1	155.3	104	7.0	138,750	40
7 days postoperative	.433	57.3	73.0	142.4	116	7.0	172,050	35
10 days postoperative	.424	35.6	86.9	174.6	113	7.0	210,900	36
15 days postoperative	.409	58.1	87.1	160.8	139	7.0	210,900	43

*A debridement of a large area of chronic osteomyelitis of the mandible was carried out in this 50 year old white man. He showed a less pronounced "fast" response and was the only patient who showed no postoperative elevation in the thromboplastic plasma component.

Table 3 • Results of tests in Case 10*

Sample	Fibrinogen (Gm. per 100 ml.)	Thromboplastic component (u/ml.)	Prothrombin (u/ml.)	Antithrombin globulin (u/ml.)	Fibrinogen conversion index	Lee-White clotting time (min.)	Platelets (per cubic mm.)	Hematocrit
Preoperative	.248	170.6	80.0	167.9	145	10.0	228,000	47
1 day postoperative	.271	172.2	82.4	158.0	159	10.0	182,450	47
3 days postoperative	.260	229.2	84.8	182.0	165	10.0	185,100	46
7 days postoperative	.249	245.8	81.4	171.2	137	10.5	245,000	45
10 days postoperative	.233	181.2	82.2	164.6	140	10.0	241,000	46
15 days postoperative	.220	174.6	80.8	172.2	142	10.0	229,400	46

*This 24 year old white man required surgical removal of two impacted mandibular third molars. He showed a "slow" response. He experienced difficulty with oozing from the extraction sites for two days after surgery.

(50 per cent), the fibrinogen conversion index increased 35 per cent by the third postoperative day and was still elevated on the tenth day. However, antithrombin globulin also rose (61 to 74 per cent) in this patient.

■ *Discussion*

The results of this study demonstrate that surgery does alter coagulability of blood. Several investigators using modifications of gross coagulation times have reported increased coagulability of blood after trauma.[1-11] Others have noticed that blood clotting becomes prolonged.[12-18] DeTakats, using an in vitro heparin sensitized clotting time,[34-36] noted two types of response after trauma or stress: prolonged coagulation and tendency to shortened coagulation.[37-39] He found the peak change of prolonged coagulability occurred on the third postoperative day. The peak shift of the fibrinogen conversion index was also found to occur on the third postoperative day.

Clinical factors were compared with differences in coagulability. It was found that the degree of surgical trauma is most important in determining the type of coagulation change. More severe surgery produces a tendency to faster coagulability. Less severe surgery produces a tendency to slower coagulability.

In addition to the fibrinogen conversion index, other laboratory tests were performed and attempts made to relate them to shifts in coagulability. Lee-White whole blood clotting times and Quick one-stage prothrombin tests showed no significant deviations even on the days when fibrinogen conversion indexes demonstrated peak changes. The limitations of clotting time tests have been discussed.[40, 41] Prothrombin likewise exhibited little deviation from day to day in the different patients. Some investigators[42] report a postoperative increase, some a decrease,[43-46] some no significant change.[8, 47, 48]

Platelet counts obtained in this study

agree in general with those of other investigators.[49-62] There is a fall for the first three or four days followed by a rise between the fourth and eighth days. The rise persists until the twelfth or fifteenth day. This trend was the same in all patients studied.

Nearly all investigators [5-9, 63-69] agree that there is a postoperative rise in fibrinogen concentration. In this study, fibrinogen concentration rose postoperatively in all but one patient. When fibrinogen concentration changes of all patients were averaged, it was observed that there was a sharp rise to 40 per cent above the preoperative value at one day and to 49 per cent (.139 Gm. per 100 ml.) at three days. The concentration then decreased slightly and leveled off to 31 per cent at the seventh and tenth days. At 15 days the fibrinogen concentration was 10 per cent above the preoperative level. The observation that fibrinogen concentration after oral and orthopedic surgery increased regardless of the change in the fibrinogen conversion index is most important. It indicated that the postoperative increase of fibrinogen concentration is a response of the inflammatory process and is not associated with rate of coagulation.

It has been shown that the thromboplastic plasma component concentration does rise after surgery in most patients. However, the fact that it also increased in a patient who had postoperative increases in the fibrinogen conversion index raises the question that, like fibrinogen, the rise may be a manifestation of the inflammatory process rather than a cause of hypercoagulability.[70]

The varying increases and decreases in antithrombin as determined in this study have been noted by other authors.[71-75] These fluctuations may be part of the body's attempt to balance the complex clotting mechanism. However, findings in this study suggest that determinations of a single coagulation factor cannot indicate the state of the entire clotting mechanism. There are apparently many different reasons for variations in antithrombin globulin, thromboplastic plasma component and platelets. This fact is evident when it is realized that blood coagulation is a complex mechanism involving many factors and equilibria. The fibrinogen conversion index seems to overcome these difficulties. It does not rely on changes of any single factor. Instead, it measures the net effect of all factors.

■ *Summary*

Serial laboratory tests were carried out preoperatively and postoperatively on patients undergoing oral or orthopedic surgery. It was found that surgery does affect the coagulability of blood as demonstrated by changes in the fibrinogen conversion index. More severe surgery produced a tendency to increased coagulability. Less severe surgery produced a tendency to decreased coagulability. Plasma fibrinogen and thromboplastic plasma component concentrations showed definite elevations after surgery regardless of the alteration in coagulability. Lee-White whole blood clotting times, modified Quick one-stage and quantitative prothrombin determinations indicated no significant deviations. Variations in platelet count and antithrombin titers could not be correlated with the shifts in coagulability.

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Bone repair after experimentally produced defects

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Three methods for the removal of bone in oral surgical procedures were evaluated as to time required to remove necessary bone and the speed of healing postoperatively. The instruments used were an engine driven mallet, an ultrasonic device and a bur rotating at high speed. In this controlled experiment in dogs, equal specimens from the mandible, below the apex of the teeth, were removed with each instrument at two days, two weeks and eight weeks after surgery. Serial sections were examined for evidence of healing. The results showed the air turbine instrument to have all the necessary qualifications for removing bone; it is gentle in its action and extremely precise.

Is there one "best" method for the removal of bone in oral surgery? What criteria should be set in evaluating the various methods?

Three factors are of prime importance:

1. The repair of the injured bone. Does the bone heal better after the use of one instrument than another?

2. How long does it take to perform the operation?

3. How much physical and psychological trauma does each method produce?

Three instruments were studied: An

Fig. 1—Three areas of bone removal. A, air turbine unit. I, Impactor. U, ultrasonic device

engine-driven mallet, an ultrasonic device and a bur rotating at high speed.

■ *Materials and Methods*

The three instruments tested in this investigation were as follows:

1. Engine-driven mallet (Impactor[1]). It is driven by an electric dental engine. An attached high carbon steel chisel cuts the bone.

2. Ultrasonic instrument (Cavitron[2]). This instrument utilizes high frequency vibration of 29,000 cycles per second. The cutting instrument was a no. 15 Bard Parker knife blade.

3. Super speed rotational instrument (Weber Air Turbine Unit[3]). This instrument is an air turbine type capable of free running speeds in excess of 200,000 rpm. The cutting instrument was a no. 59 carbide smooth fissure bur.

With the exception of the instrument used, all surgical procedures were the same. Cutting operations were carried out under isotonic, isothermal saline irrigation. The time required to remove a similar section of bone was recorded.

Three young healthy dogs were used in this study. They were anesthetized with intravenous veterinary thiopental sodium. A horizontal incision was made in the mucous membrane of the mandible, 5 mm. below the attached gingiva. The incision extended from the third molar to the canine tooth. A flap was retracted inferiorly and three separate regions of bone approximately 4 mm. square and 4 mm. deep were removed with each instrument. The experimental regions were in the mandible below the apexes of the molar teeth (Fig. 1). The flap was then approximated and sutured with no. 000 chromic suture. A similar procedure was carried out on the opposite side of the mandible.

Specimens were taken two days, two weeks, and eight weeks after surgery. The operated region of the mandible was resected and fixed in Formalin for five days. Roentgenograms were then taken. The specimens were decalcified, sectioned and stained with hematoxylin and eosin.

■ *Results*

No significant roentgenographic difference was noted two days and two weeks after the operation (Fig. 2, 3). Eight weeks after surgery the roentgenograms showed a greater density in the area which had been removed with the air turbine unit than in the areas removed with the other instruments (Fig. 4).

Serial sections across each surgical injury were examined with a light microscope for evidence of healing.

IMPACTOR—Two days after the surgery, the region from which the bone had been removed with the engine-driven

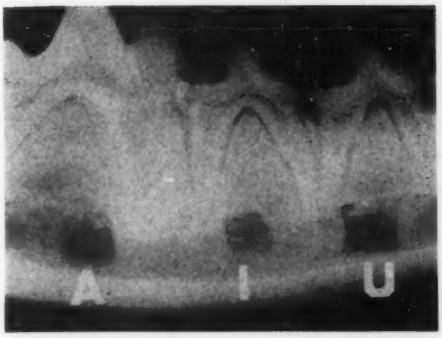

Fig. 2—View taken of specimen two days after surgery. A, air turbine unit. I, Impactor. U, ultrasonic device

Fig. 3—View taken of specimen two weeks after surgery. A, air turbine unit. I, Impactor. U, ultrasonic device

Fig. 4—View taken of specimen eight weeks after surgery. I, Impactor. U, ultrasonic device. Arrow points to region removed with air turbine unit

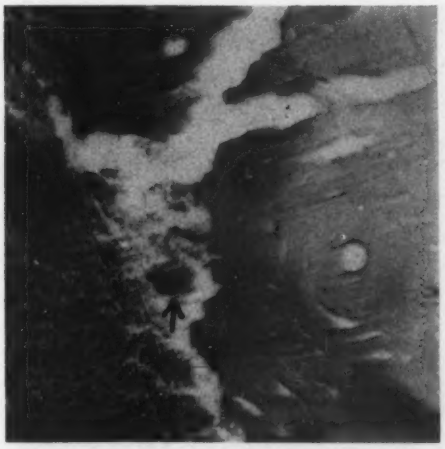

Fig. 5—Section of a two day specimen cut with Impactor. Arrow points to bone chips. Note slight basophilic zone at margin of cut bone

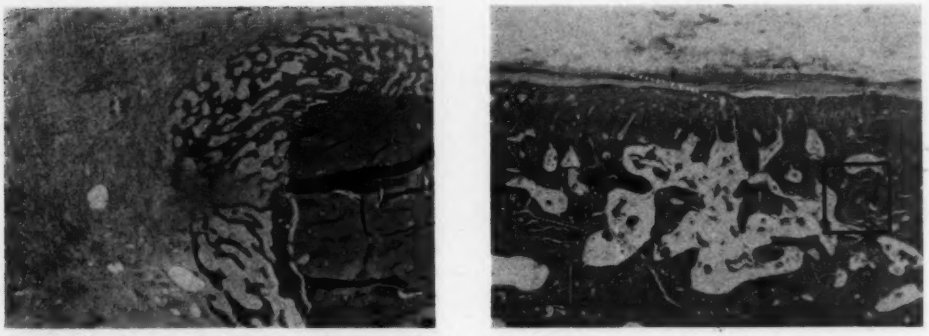

Fig. 6—Left: Section of two week specimen cut with Impactor. Repair bone from periosteum in apposition to cut surface. Right: Eight week specimen of operative site cut with Impactor, showing repair

mallet had filled with an organized blood clot. Mild inflammation was present. Numerous fragments of bone were close to the cut surface which was lacerated and exhibited a definite basophilic zone that varied in depth (Fig. 5).

Bone repair was evident in two weeks. The primary source was from the periosteal surface lateral to the edge of the wound. Trabeculae of new fibrillar bone also originated from the endosteal surface and in a few regions attached to the cut surface of bone. Repair bone formed around the fragments which were located near the cut surface. Dense connective tissue with a mild lymphocytic infiltration filled the rest of the region (Fig. 6, left).

There was evidence of new bone in apposition to the cut surface, except in regions where the basophilic zone was present. The basophilic zone showed no resorption.

After eight weeks the region was filled primarily with cancellous bone. Portions of the cut surface were resorbed and there was apposition of new bone almost completely across it (Fig. 6, right). In a few isolated regions the basophilic zone was still evident. There was no resorption of the basophilic surface nor was there any apposition of new bone (Fig. 7).

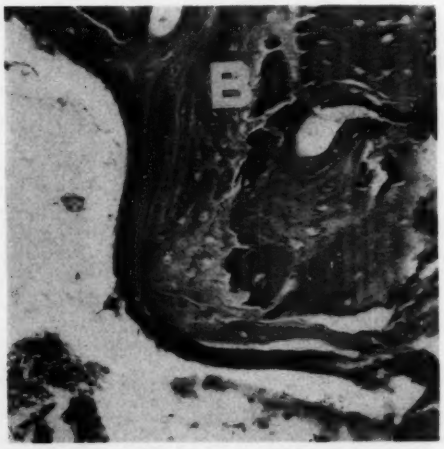

Fig. 7—Higher magnification of box in Figure 6, right. Note lack of apposition of new bone to lacerated basophilic margin of cut bone

Numerous particles of necrotic bone which had been fragmented at surgery

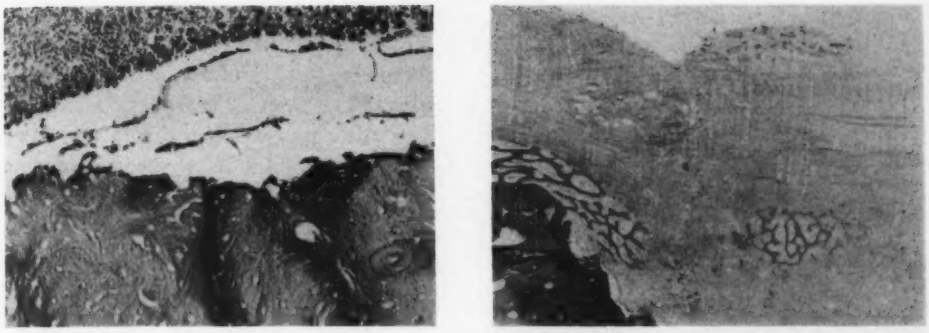

Fig. 8—Left: Two day specimen of bone cut with ultrasonic device. Note basophilic surface. Right: Two week specimen cut with ultrasonic device. New bone arises lateral to margin of injury. Note basophilic lacerated surface of cut bone

were within the mass of bone filling the injury.

ULTRASONIC INSTRUMENT—The cut edge of bone of the two-day specimen taken from the region cut with an ultrasonic instrument showed a variable stained zone along the cut surface (Fig. 8, left). It was wider than the similar zone shown in Figure 5. The clot showed organization with a moderate polymorphonuclear infiltration.

After two weeks the region was filled with dense connective tissue and there was moderate lymphocytic inflammation. From the periosteal surface, trabeculae of bone swept into the injured portion. The cut surface retained its deep basophilic character; there was no new bone in apposition to the cut surface (Fig. 8, right).

After eight weeks the void was partially filled with haversian bone which had arisen from the periosteal surface. The darkly stained basophilic zone on the cut surface of bone was still present (Fig. 9, left). Bone resorption occurred in a

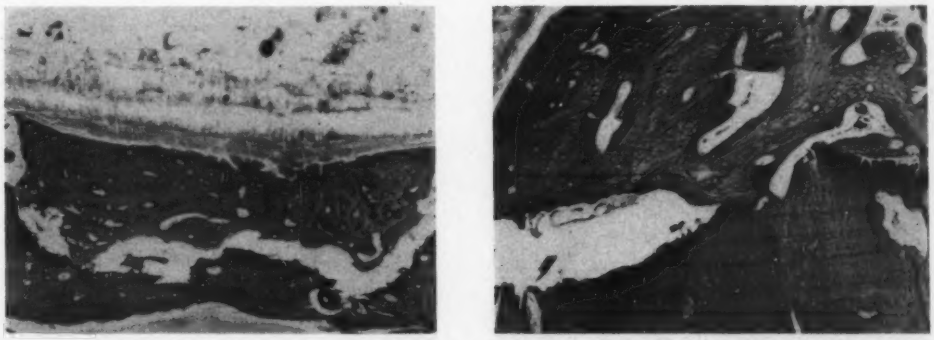

Fig. 9—Left: Eight week specimen cut with ultrasonic device. Note lack of apposition of new bone to basophilic zone. Right: Higher magnification of another eight week specimen cut with ultrasonic device. Note lack of resorption of basophilic zone and failure of apposition of new bone against basophilic surface

Fig. 10—Two day specimen of bone cut with air turbine type instrument. Note smooth cut surface and minimal basophilic zone

few isolated regions and new bone was in apposition (Fig. 9, right).

AIR TURBINE TYPE INSTRUMENT—The two day sections taken from the region cut with the air turbine type instrument showed a smooth cut margin with a minimal basophilic border. The wound was filled with an organizing clot in which there was evidence of mild polymorphonuclear leukocytic inflammation (Fig. 10).

After two weeks the void was filled with dense fibrous elements showing young bone formation. There was new bone formation in apposition to the cut surface which was trabecular and the location of the osteoblasts indicated that the bone arose from the periphery to occupy the region of the wound. It was difficult to detect a definite basophilic zone (Fig. 11, left).

After eight weeks the operated region was primarily filled with compact haversian bone that was in firm apposition to the cut surface (Fig. 11, right). There was a noticeable lack of a basophilic zone on the original cut surface of bone. There was slight evidence of resorption on the originally cut surface (Fig. 12).

EFFECTIVENESS OF INSTRUMENTS—Each complete surgical procedure from the initial incision to the final closure took approximately 15 minutes. The aver-

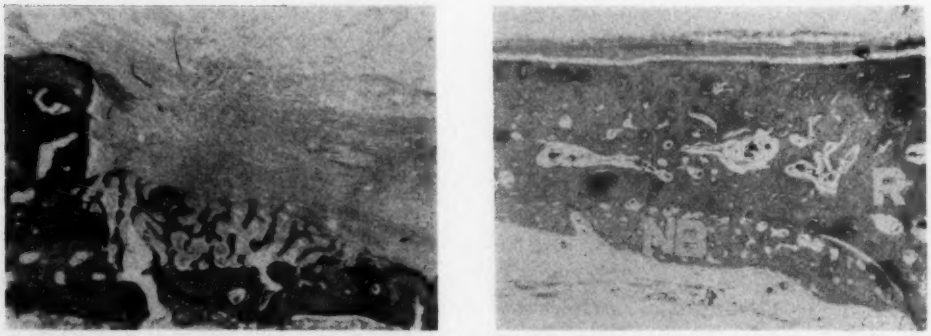

Fig. 11—Left: Two week specimen of bone cut with air turbine type instrument. Note bone repair in apposition to cut surface. Right: Eight week specimen of operative site cut with air turbine type instrument. NB, new supporting bone formation opposite injured area. R, repair area in apposition to cut surface

age time of bone removal with each instrument was (1) air turbine type—25 seconds; (2) engine-driven mallet—40 seconds; (3) ultrasonic device—139 seconds.

■ *Basophilic Surface of Cut Bone*

The basophilic zone at the cut surface of bone is significant in repair. In the present study it was noted that a similar basophilic zone was found at the edge of the bone which had been cut with a razor blade after decalcification. In this instance it was shallow. A pilot study was undertaken to investigate further the basophilic surface of cut bone.

A dissected rat femur was fixed in Formalin. A cut was made with a saw below the head about half the thickness of the shaft. It was then decalcified and the condylar end was removed with a razor blade. The femur was sectioned and stained with hematoxylin and eosin.

Examination of the saw cut showed a basophilic zone on the cut surface (Fig. 13, left). The surface cut with a razor blade after decalcification showed a narrower basophilic zone along the edge (Fig. 13, right). It was deducted, therefore, that the basophilic zone was a physical phenomenon related to the cut bone surface.

Fig. 12—Higher magnification of an eight week specimen cut with air turbine type instrument. New bone formation in apposition to cut surface

■ *Discussion*

The engine-driven mallet (Impactor) is very similar in action to the mallet

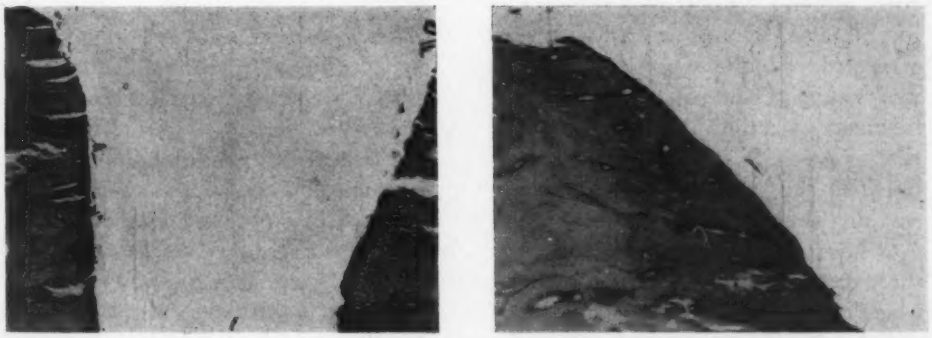

Fig. 13—Left: Basophilic zone in rat femur cut with a saw after fixation. Right: Basophilic zone in rat femur cut with razor blade after decalcification

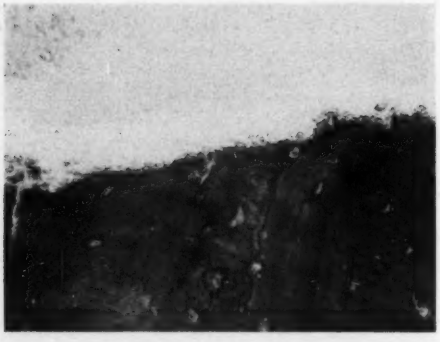

Fig. 14—Specimen showing basophilic zone which contains viable osteocytes

and chisel. It has been described as an excellent instrument for removing bone.[4] The operator, by controlling the speed of the engine, can vary the frequency of the blows imparted to the attached chisel point. Because the bone was removed by the impact of a chisel, it was accepted as a standard for the mallet and chisel in this study. The main disadvantage of the engine-driven mallet in clinical use is the psychological and physical trauma to which the patient is subjected.

Oral surgeons have recognized the problem and have sought a way to reduce or eliminate these undesirable aspects of bone surgery. With the introduction of the ultrasonic instrument, the trauma associated with the engine-driven mallet was virtually eliminated.[5,6] This high frequency vibration produces a gentle cutting action. It is claimed that in some instances the patient is "unaware that anything is being done."[5]

The ultrasonic device used in this study proved to be the least effective when compared with the engine-driven mallet and a high rotational cutting instrument.

The process of repair after its use definitely was inhibited. There was no evidence of endosteal bone originating from the cut surface. Apposition of new bone against the deeply stained cut surface occurred only in a few small regions. More noticeable was the lack of apposition against these stained areas and lack of resorption.

The ultra-high-speed rotational instrument has all the necessary qualifications for removing bone. It is gentle in its action and extremely precise. It has been shown to be 30 per cent more effective than other methods commonly employed to remove bone.[7,8] The present study showed that the instrument removed bone faster than the engine-driven mallet or ultrasonic instrument.

More significant was the pattern of healing. The apposition of new bone to the cut surface and the rate of repair was enhanced when the air turbine unit was used. After eight weeks the region of repair had returned almost to its normal anatomic form.

INTERPRETATION OF THE BASOPHILIC ZONE—The basophilic zone is of particular interest. It is resistant to resorption and bone apposition. Since these two phenomena are associated with the repair process, it deserves special consideration.

In the present study the basophilic surface varied in depth according to the instrument used in the surgical procedure. It was obvious that the smoother the cut surface, the less deeply stained was the region. It was also obvious that the repair process was enhanced with a smooth cut bone surface. The nature of this surface is worthy of investigation.

The basophilic zone could be produced in chemically fixed bone. It even occurred if bone was cut after decalcification. It is inconceivable that cutting decalcified bone with a razor blade will produce a burned surface. In the region of the basophilic bone there were viable osteocytes (Fig. 14).

It is evident, then, that the basophilic zone is a staining phenomenon. The staining of tissue with hematoxylin and eosin is accomplished by surface absorption.[9] This phenomenon is related to the qualitative and quantitative nature of the surface.

Since the qualitative characteristics of the rat bone remain unchanged, the increased staining phenomenon, in this instance, must be quantitative in nature.

By increasing the surface area, as in etching, more sites for absorption of dye were created. This produced a surface which stained darker. The same principle would apply to a surface which was roughened or lacerated.[10] By creating a rough or lacerated surface at the cut edge of bone, more sites are available for absorption and a greater staining intensity will result. This affords a possible explanation for the basophilic zones which still contained osteocytes noted in the various histologic sections.

The study herein described established that a smooth surface is conducive to repair. Since the smoothest surface and best repair occur when the bone removal is with a rapidly revolving smooth fissure bur, it is undoubtedly the instrument of choice. In contrast, the rapidly vibrating Bard Parker blade as used with an ultrasonic device produces the most lacerated surface as is shown by the wide basophilic zone. The subsequent repair is inhibited.

The results achieved by the use of the engine-driven mallet lie somewhere between those resulting from the use of the other two, as measured by the surface roughness. In addition, there was fragmentation of the bone. Although no sequestrums were observed, this possibility is real, and the desirability of bone fragments has yet to be established. This study did not indicate there was any advantage to bone chips in the region.—*125 West Twenty-first Street.*

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Plasma cholinesterase and the duration of succinylcholine-induced apnea

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To understand better the pharmacology of succinylcholine an experiment was designed to measure the response in normal dogs receiving various levels of plasma pseudocholinesterase and a standard dose of succinylcholine. The accumulated evidence indicated that the response to standard doses of succinylcholine is related to the plasma pseudocholinesterase activity, but the actual plasma level of pseudocholinesterase probably acts in a secondary manner in determining the degree of succinylcholine sensitivity.

Succinylcholine is a muscle-relaxing agent that has clinical properties which make it almost ideally suited for use in anesthesia. However, many aspects of the physiological action of this agent remain obscure, especially its rather infrequent but distressing prolonged action. This sensitivity, notably expressed by a sustained respiratory depression or apnea, cannot be explained on the basis of dosage alone. The effect of a pseudocholinesterase administered before and after use of succinylcholine was studied.

■ *Methods and Materials*

Mongrel dogs, lightly anesthetized with an intravenous barbiturate preparation, were used for experimentation. The animals were intubated with a cuffed endotracheal tube which was connected by a glass "Y" connector to a positive-negative type resuscitator and to a rubber diaphragm type tambour. A writing lever attached to the rubber diaphragm of the tambour was allowed to scribe on a slow-moving kymograph drum. It was noted that this recording device gave a very good record of the slightest respiratory movement and of the rate of respiration, but only a rough estimation of the depth of respiration. From these records and from those of a timing device recording simultaneously, the respiratory response to succinylcholine could be determined.

Apnea time as a response to succinylcholine was taken and was determined as that period of time during which the animal showed no respiratory movement. The animals were administered 100 per cent oxygen under no pressure for three minutes prior to relaxation. During the period of apnea or definite respiratory depression, the animals were ventilated by positive pressure twice followed by one minute of oxygen under no pressure. This cycle was repeated as long as the dogs were unable to breathe adequately for themselves. The method may be open to

criticism with regard to possible hypoxia and hypercapnia. However, no great changes were observed in either heart rate or blood pressure during any such 20 minute period that would indicate any adverse effect from the conditions mentioned.

An indwelling Cournand needle was inserted into one of the femoral arteries. This was attached to a reservoir type mercury manometer, from which mean arterial blood pressures could be recorded. The arterial needle also allowed easy collection of blood samples which were taken at various intervals throughout the experimental period. Apical heart rates were taken by the use of a stethoscope.

The gasometric method of Barcroft and Warburg as modified by Ammon[1] was used in this investigation for estimation of cholinesterase activity of the blood samples. Butyrylcholine, as paratoluene sulfonate in 0.02 molar concentration, was used for pseudocholinesterase determinations, and acetyl-β-methylcholine in 0.03 molar concentration was used for true cholinesterase determination. The amount or level of plasma pseudocholinesterase is expressed in terms of activity with its appropriate substrates, and is recorded in microliters of carbon dioxide evolved by 1 ml. of plasma in one minute (μl. CO_2/ml./min.)

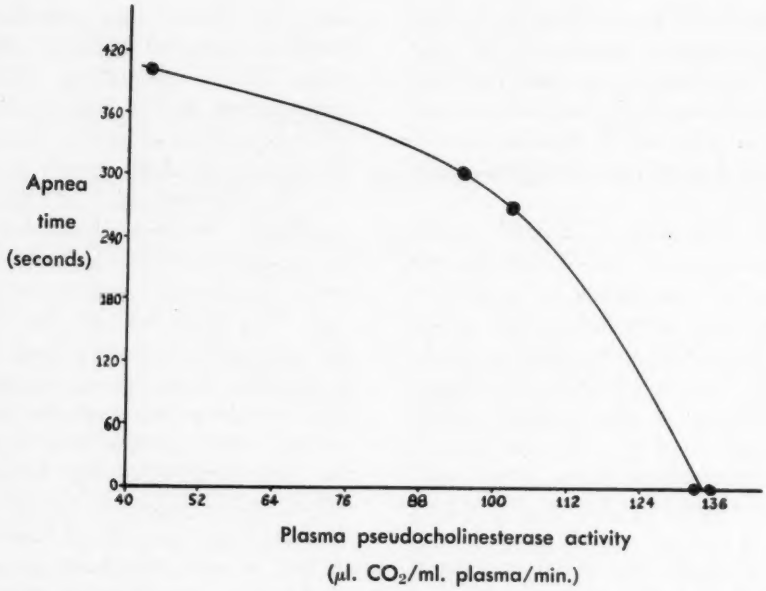
The pseudocholinesterase preparation is prepared from human serum by fractional precipitation, preserved in sterile containers and kept at low temperatures. Each cubic centimeter contained the pseudocholinesterase activity of 350 cc. of plasma. Preliminary assays on the pseudocholinesterase preparation indicated that each cubic centimeter contained an average of 29,820 microliters of carbon dioxide per minute of pseudocholinesterase activity and an average of 196.8 microliters of carbon dioxide per minute of true cholinesterase activity.

The dogs were bled and then given transfusions of plasmapheresed blood in the experimentation to lower the plasma pseudocholinesterase activity in the animals. This blood was prepared by separating the cells from the plasma of fresh donor dogs' blood by centrifuging. The cells were then washed one time with 0.9 per cent saline solution, centrifuged, and the supernatent discarded. Immediately before use, the cells were restored to the original volume of collected blood by the addition of 6 per cent plasma expander in saline solution to which had been added predetermined amounts of salts and glucose. The plasma pseudocholinesterase activity of such treated blood decreased 91.1 to 100 per cent, and the plasma true cholinesterase activity decreased by 86.1 to 94 per cent.

■ *Experimentation and Findings*

The objective of the experimentation was to observe the response to succinylcholine in dogs with various levels of plasma pseudocholinesterase.

REACTION TO SUCCINYLCHOLINE AT NORMAL LEVELS OF PLASMA CHOLINESTERASE—The reactions of a group of animals to standard doses of succinylcholine (0.1 mg./kg. of body weight) appeared to be related to the pseudocholinesterase levels. Greater sensitivity was noted in animals having a lower activity of plasma pseudocholinesterase (illustration).



Effects of standard amounts of succinylcholine on five dogs, at normal plasma pseudocholinesterase levels

In those animals in which the plasma true cholinesterase level was determined, no relationship between plasma level and response to succinylcholine could be noted.

Preliminary studies using varied doses of succinylcholine gave evidence of a direct dose-response relationship, in that larger doses of the relaxant invariably resulted in longer periods of apnea in any individual animal.

REACTIONS TO SUCCINYLCHOLINE AT LOWERED LEVELS OF PLASMA CHOLINESTERASE—After blood samples were taken and the animals were tested for initial responses to succinylcholine, hemorrhages were induced through the arterial needle. The blood volume was calculated to be 80 ml. per kilogram of body weight, and approximately 40 per cent of the total volume was removed, with extremes of 33 and 62 per cent. At once, equal volumes of the prepared, plasmapheresed blood were rapidly administered intravenously under pressure. After a short period for stabilization, the procedures were repeated. Extremes of 600 to 1,000 ml. of blood were substituted by this method. The average for five dogs was 885 ml. A transient hypotension occurred during the blood substitution, but the dogs showed no ill effects from this operation throughout the remaining experimental period or during the following day.

The animals showed an average decline in plasma pseudocholinesterase activity of 69 per cent with extremes of 56

and 74 per cent. Inasmuch as the erythrocyte volumes were relatively unchanged and since the true cholinesterase is bound to the stroma of the erythrocyte,[2] no alterations in their true cholinesterase activity would be expected, although this possibility was not explored.

It is immediately obvious that lowering of the plasma pseudocholinesterase by this method was not reflected in any prolonged responses or sensitivities of the animals to succinylcholine (Table 1).

Table 1 • Effect of plasmapheresis on succinylcholine sensitivity

Number of dogs tested	5
Average serum pseudocholinesterase	123.66
Average apnea time* after succinylcholine 0.1 mg./kg.	169
Average blood substitution (ml.)	885
Average serum pseudocholinesterase after blood substitution	37.96
Average apnea time after succinylcholine 0.1 mg./kg.	178

*Apnea times are recorded in seconds, cholinesterase levels recorded in μl. CO_2/ml./min.

REACTIONS TO SUCCINYLCHOLINE AT ELEVATED LEVELS OF PLASMA CHOLINESTERASE—The effects of raising the plasma pseudocholinesterase levels by intravenous injections of concentrated human plasma cholinesterase before administration of succinylcholine were uniform and an inverse relationship was indicated by the results. As the plasma pseudocholinesterase activity was elevated, there was a definite decrease in the sensitivity of the animal to succinylcholine, as shown by a decrease in the apnea times (Table 2).

At least two choline-splitting enzymes are known to exist in the blood of most species.[3] The first is known as "acetylcholinesterase,"[4] "specific" cholinesterase[5] or "true" cholinesterase.[6] This enzyme is found in various tissues of the body. In the blood it is found in the plasma and, more abundantly, bound to the stroma of the erythrocytes. According to the hypothesis of chemical transmission, destruction of acetylcholine by true cholinesterase at the nerve endings prevents a paralyzing action of acetylcholine, and allows the muscle cell membrane to repolarize. The second of the choline splitting enzymes is "cholinesterase"[4] or "pseudocholinesterase."[6] This enzyme is also capable of hydrolyzing acetylcholine but it does so at a rate lower than that by true cholinesterase. Pseudocholinesterase is found in varying concentrations throughout the body tissues, whereas in the blood it is found only in the plasma.[3] At the present time, no conclusive evidence has been presented for the function of pseudocholinesterase, and its physiological substrate is unknown, although it is known to hydrolyze succinylcholine in the blood rapidly.

Succinylcholine, which is used in the form of dicholine, is classified as a constant depolarizing agent, in which role it acts like acetylcholine. The relaxant, however, has been shown to have an anticholinesterase action. Although it is not hydrolyzed by true cholinesterase, succinylcholine does inhibit the hydrolysis of acetylcholine by both pseudo and true cholinesterase.[7]

There are many conceivable modes by which succinylcholine may cause prolonged muscular weakness or apnea: by central effect, either through a direct action of the drug on the respiratory center or by resultant anoxia, hypocapnia or excessive hypercapnia; by accumulation of succinyl-monocholine which is an inter-

Table 2

Examples of the effect of plasma cholinesterase levels on succinylcholine sensitivity

Clock time	Remarks and results	
	Dog 2, 13.7 kg.	
1:45	Pseudocholinesterase activity*	94.6
2:05	Succinylcholine, 2.04 mg./kg.	
	Apnea time (seconds)	1,029
2:42	Pseudocholinesterase, concentrated, 1 ml.	
2:52	Pseudocholinesterase activity	144.5
2:58	Succinylcholine, 2.04 mg./kg.	
	Apnea time (seconds)	646
3:22	Pseudocholinesterase, concentrated, 1 ml.	
3:29	Pseudocholinesterase activity	196.8
3:38	Succinylcholine, 2.04 mg./kg.	
	Apnea time (seconds)	399
	Dog 7, 15.5 kg.	
10:58	Pseudocholinesterase activity	42.4
	True cholinesterase activity	1.45
11:18	Succinylcholine, 0.1 mg./kg.	
	Apnea time (seconds)	354
11:34	Pseudocholinesterase, concentrated, 1 ml.	
11:39	Pseudocholinesterase activity	115.4
	True cholinesterase activity	1.62
11:42	Succinylcholine, 0.1 mg./kg.	
	Apnea time (seconds)	60
11:53	Pseudocholinesterase, concentrated, 1 ml.	
11:59	Pseudocholinesterase activity	115.9
	True cholinesterase activity	1.89
12:00	Succinylcholine, 0.1 mg./kg.	
	Apnea time (seconds)	None

*Cholinesterase activities are expressed in μl. CO_2/ml./min.

mediate product of succinyl-dicholine hydrolysis and is a weak depolarizing agent;[8] by acidosis which results in decreased alkaline hydrolysis of succinylcholine,[9] by inhibition of true cholinesterase by succinylcholine, thus permitting the sustained action of acetylcholine at the end plate region; or by decreased succinylcholine destruction, as a result of a lowered pseudocholinesterase activity of the plasma or tissues.

A decreased level of plasma pseudocholinesterase is not unusual, especially in patients with poor health.[10] Administration of a concentrated pseudocholinesterase preparation before production of relaxation by succinylcholine has been shown to decrease the sensitivity to the muscle relaxant.[11,12] There are indications, however, that this preparation will not decrease the sensitivity to succinylcholine if it is given while the patient is exhibiting prolonged respiratory depression.[13]

Nishikawara[14] has presented clinical evidence that the plasma activity of pseudocholinesterase, although directly related to the level in the liver, was not an index of a tissue level (intestinal mucosa). From this information and from the knowledge that the concentrated human plasma pseudocholinesterase used in this experiment is bound globulin, it is possible to justify the assumption that the extra vascular levels of pseudocholinesterase were not altered greatly in the animals during the preceding experimentation.

Artificial lowering of the plasma pseudocholinesterase level in the animals

by plasmapheresis is not reflected by an increase in the animals' sensitivity to succinylcholine. This suggests a possibility that plasma pseudocholinesterase may act in only a secondary manner in the hydrolysis of succinylcholine; namely, the hydrolysis of free succinylcholine in the blood stream.

Elevation of the level of plasma cholinesterase by administration of concentrated human plasma pseudocholinesterase decreased the sensitivity of the animals to succinylcholine. This suggests that, at higher levels, plasma pseudocholinesterase may also act to limit the amount of succinylcholine that can reach the end plate region. Although plasma pseudocholinesterase apparently acts in a secondary role in true succinylcholine sensitivity, it would appear to be of primary importance in determining the dosage for any individual patient.

Relegation of plasma pseudocholinesterase to a secondary role in true succinylcholine sensitivity necessarily must follow some assumption on the primary factors in such sensitivities. It would seem reasonable to suggest that patients who are exceptionally sensitive to succinylcholine are those with low tissue cholinesterase levels or those patients in whom the mechanisms involving the destruction of succinylcholine at the end plate regions are impaired. It is interesting to note, however, that Koelle[15] reported that only small traces of pseudocholinesterase are found at the myoneural areas of the muscles.

■ *Conclusions*

1. The response to standard doses of succinylcholine in normal dogs is related to the plasma pseudocholinesterase activity.

2. The plasma level of pseudocholinesterase apparently acts in a secondary manner in determining the degree of sensitivity to succinylcholine. This occurs possibly by hydrolyzing the free succinylcholine and by limiting the amount of succinylcholine that will reach the myoneural junction.

3. It is possible that true sensitivity to succinylcholine is related to tissue factors.—*1017 Market Street.*

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Cholase, the pseudocholinesterase preparation used in this study, was supplied by Cutter Laboratories.

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The influence of epinephrine on the incidence of bacteremia

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The effect of varying concentrations of epinephrine in local anesthetic solutions on the incidence of bacteremia in 73 patients was studied. A diagnosis of bacteremia was made only when at least twice as many microorganisms were found in the postoperative sample as in the preoperative blood sample. Nine of 73 patients developed bacteremia after extractions. There was no apparent difference in the incidence of bacteremia after the use of epinephrine-free solution and the solution using 1:100,000 epinephrine. The incidence of bacteremia increased when extractions were performed in unhealthy mouths.

The difference in the incidence of bacteremia under similar operating conditions has led to the assumption, since 1937, that epinephrine as a vasoconstrictor in local anesthetic solution reduces the incidence of bacteremia after tooth extraction.[1]

The principal factors known to influence the incidence of bacteremia are the number of teeth removed, the degree of surgical trauma, the time involved in the operation and the presence of concurrent infection.[2-9]

The purpose of this investigation was to determine the influence of epinephrine on the incidence of bacteremia. The results question the traditional belief that epinephrine is significant.

■ *Materials and Methods*

PATIENTS—Several hundred patients who came to the dental clinic at the Ohio State University for tooth extraction were screened. A pertinent medical history was taken from each patient and roentgenograms were made of all teeth to be extracted. Patients were rejected if they had nose or throat infection, acute or chronic pyogenic infection other than oral, or a history of antibiotic therapy for the preceding six months. Seventy-three patients qualified.

The patients were divided into the following three general categories relating to oral health. Good: Good professional and home care; clinically normal gingivae; no obvious carious lesions. Fair: Inadequate professional and home care; mild gingival inflammation; minimal carious lesions. Poor: Complete lack of professional and home care; advanced periodontal disease; gross carious lesions.

ANESTHETIC SOLUTIONS—A 2 per cent local anesthetic agent was used. The investigator did not know the concentration of epinephrine used as a vasoconstrictor. Three different solutions were prepared. One contained no epinephrine, the second contained epinephrine 1:100,000, and the third contained epinephrine 1:50,000. These solutions were identified only by number until the final results were tabulated.

Each patient received between 2 and 3 ml. of the anesthetic solution.

SURGERY — Senior dental students gave the injections and performed the surgery under the personal supervision of the author.

The maximum time allowed for the surgical procedure was two minutes. Where indicated, a second tooth was removed if the original anesthesia was adequate for the extraction and the procedure could be done within two minutes.

Patients were rejected if the time limit was exceeded, if a tooth was fractured during extraction, or if there was excessive trauma in the opinion of the author. Five patients originally admitted to the experimental group were disqualified for these reasons at the time of surgery. Sixty-eight, ranging in age from 16 to 54 years, remained in the study.

PROCEDURE—The antecubital region was prepared with tincture of nitromersol and 70 per cent alcohol, and a preoperative sample of 15 ml. of blood was withdrawn. This sample was placed in an Erhlenmeyer flask which contained 1.5 ml. of 4 per cent sodium citrate to prevent coagulation.

The patient used a solution of cetyl pyridinium chloride as a mouthwash for a full minute before the injection. This is a routine procedure at the oral surgery clinic. The technic of injection was either primary conduction or infiltration.

The soft tissues were separated from the tooth and the extraction was completed with a forceps. Immediately after the extraction, a 25 ml. blood sample was withdrawn over a period of 40 to 60 seconds. This sample was placed in 3 ml. of citrate solution.

BACTERIOLOGIC PROCEDURE—The following procedure was used to establish evidence of bacteremia.

Preoperative blood sample: 0.1 ml. was streaked on each of four blood agar plates. Two plates were cultured aerobically and two anaerobically; 5.0 ml. were pipetted into each of two flasks containing 50 ml. of brain-heart infusion broth; 1.0 ml. was pipetted into a test tube of thioglycollate broth as a test for sterility.

Postoperative blood sample: 0.1 ml. was streaked on each of four blood agar plates, as in the preoperative blood sample; 10.0 ml. were pipetted into each of two flasks of 100 ml. brain-heart infusion broth; 1.0 ml. was pipetted into each of two test tubes of thioglycollate broth.

The inoculated cultures were incubated at 37°C. for seven days. As a control, a noninoculated sample of each batch of media was cultured under the same conditions. The cultures were examined daily.

Turbidity was regarded as evidence of bacterial growth and when it appeared, subcultures were prepared on blood agar plates. From those plates on which growth

Table 1 • Relation of epinephrine concentration to postoperative bacteremia

Epinephrine concentration	Number of patients	Number positive	Per cent positive
0	20	3	15
1:100,000	35	5	14
1:50,000	13	1	8
	68	9	13

occurred, the organisms were streaked on slides, gram stained and examined microscopically. The microorganisms were identified by their colony morphology, their action on blood agar and their gram stain reaction.

SAMPLE VOLUME—A bacteremia was recognized only when the difference in volume of the preoperative and postoperative sample was accounted for. That is, diagnosis of a postoperative bacteremia was made only when at least twice as many microorganisms were found in the postoperative sample as in the preoperative sample. The quantification of bacteria was applied only as a means of validating a bacteremia. It was not used to establish a specific bacterial count.

■ *Results*

PREOPERATIVE RESULTS — Negative cultures indicated that there were no incidences of preoperative bacteremia in the total patient population.

POSTOPERATIVE RESULTS — Positive blood cultures established that nine of the 68 patients developed bacteremia after tooth extraction (Table 1).

MICROORGANISMS—The bacteria were identified and their frequency recorded. Beta hemolytic micrococci were recovered from the blood sample of two patients, and gamma hemolytic streptococci and alpha hemolytic streptococci also were recovered, each in only one instance. No mixed cultures were found (Table 2).

NUMBER OF EXTRACTIONS — There were 13 patients from whom it was possible to extract two teeth. Of these 13 patients, two developed a bacteremia. Of the remaining 55 patients who had a single extraction, seven developed a bacteremia.

ORAL CONDITION—Table 3 shows the relation of the incidence of bacteremia to the patient's oral condition.

■ *Discussion*

This investigation was stimulated by a review of the literature which led to the discovery of a great difference in the reports on the incidence of bacteremia after the extraction of teeth. Most of the published investigations[5-12] had as their basic aim the prophylactic use of chemotherapeutic agents to reduce the occurrence of postoperative bacteremia. Some of the studies[2, 8, 13, 14] were confined to determination of the sequence of events leading to subacute bacterial endocarditis. Others[1, 3, 4] were concerned with the source and frequency of bacteremias.

Okell and Elliot,[8] using general anesthesia, reported a 60.9 per cent incidence of bacteremia after the extraction of teeth. Burket and Burn,[1] using local anesthesia, reported a 16.9 per cent incidence. They considered that this reduction in frequency was caused by the fact that the local anesthetic solution contained epinephrine. Further, they said that the

mechanism of the action was vasoconstriction. Northrop and Crowley,[14] in their work on the prophylactic use of sulfathiazole, stated that the lowered incidence of bacteremia "can be attributed only to the vasoconstrictor" action of the epinephrine in local anesthetic solution.

It is well established that the action of epinephrine on the terminal arterioles and capillaries diminishes the size of the vessels; the reaction might serve to restrict the entrance of bacteria into the circulatory system. This idea would be understandable when an infiltration technic was used. However, the effect might be lessened in those instances where the site of injection was distant from the site of operation.

Some authors[1] have said that the frequency of bacteremia is greater in conduction anesthesia, whereas others[9] hold that the incidence increases with the infiltration technic. In the present study, conduction anesthesia was complemented by terminal infiltration, so no method could be devised to separate the two injection methods for analysis.

There is another possible explanation for the reduction of bacteremia after the use of local anesthesia: the direct action of epinephrine and the anesthetic agent, either alone or in combination. With the exception of Villardo,[15] who has indicated that procaine has bactericidal properties, no mention was found in the available literature concerning the antibacterial properties of either epinephrine or other anesthetic agents.

Table 3 • Relation of oral health to postoperative bacteremia

Oral health	Number of patients	Number positive	Per cent positive
Good	19	1	5
Fair	38	5	13
Poor	11	3	27

It is possible to find bacteria in small numbers in the blood of normal individuals from time to time, arising from sources not readily determined. This is not regarded generally as a pathological condition. A bacteremia may occur when the numbers of bacteria entering the circulatory system are readily detectable in quantity for an indefinite period of time. In such bacteremias the origin often may be determined.

A review of the literature showed that sample volumes of blood used to establish bacteremia varied from 5 to 23 ml., with the usual sample being 10 ml. In this study a 15 ml. preoperative sample

Table 2

Distribution of positive postoperative cultures

Microorganism	Aerobic plate	Anaerobic plate	BHI flask	Thiogly. tube
Micrococci, beta hemolytic	+*	+	+	
Micrococci, beta hemolytic	+	+	+	+
Micrococci, beta hemolytic	+	+	+	+
Micrococci, beta hemolytic	+	+	+	+
Micrococci, beta hemolytic	+	+	+	+
Streptococci, alpha hemolytic		+	+	
Streptococci, beta hemolytic	+	+		
Streptococci, beta hemolytic	+	+	+	+
Streptococci, gamma hemolytic	+	+	+	+

*Indicates growth.

of blood was considered sufficient to determine the presence of a bacteremia.

During a bacteremia after tooth extraction, it was assumed that the numbers of bacteria present in the blood stream could vary considerably. To cover a critical range in numbers of organisms and in consideration of patient tolerance to the procedure, the postoperative sample was increased to 25 ml.

The culture technic used in this study was a modification of the "multiple portion sample technique" as named and used by Robinson and his group.[4] However, prior to their work, the distribution of samples onto various media had been used by Burket and Burn[1] and Glaser and his coworkers.[9] This technic provides a better opportunity for isolating microorganisms from a blood sample than the single portion method in which the inoculum is added to a single flask of medium for culture and thereafter is subcultured at a designated time or when turbidity occurs.

Green and Dodd[16] and Richardson and Jones[17] have shown that many kinds of microorganisms can be found in human saliva. Predominant among the genera are the streptococci, the micrococci, and the gram-negative diplococci in the approximate ratio of 100:2:1, in that order. An oral surgery procedure theoretically could allow passage of any or all of the types of bacteria into the circulatory system. Identification of the microorganisms in this study was limited by time and facilities; therefore, an arbitrary selection of genera was based on consideration of predominance of microorganisms which most likely would be found in a transient bacteremia from an oral source, and those genera which would be potentially virulent.

Most previous investigations[2-14] have shown that in postextraction bacteremias streptococci occur more frequently than micrococci. In the present study the nearly even occurrence of these microorganisms cannot be explained readily.

There was no apparent difference in the incidence of bacteremia after the use of the epinephrine-free solution and the solution containing epinephrine 1:100,000. This is of major interest since anesthetic agents containing epinephrine 1:100,000 are the standard solutions in clinical use today.

The number of patients in the group receiving the solution with epinephrine 1:50,000 was small. Since only one bacteremia was recorded, it is difficult to draw a valid conclusion.

One group of authors[1,3,7] could not show a significant relationship between oral health and postoperative bacteremia. Others[8,9] maintained that such a relationship exists. The investigation sheds further light on the issue, because the results show an increase in the incidence of bacteremia after tooth extraction in the unhealthy mouth.

The incidence of bacteremia increases with the number of teeth removed at one time. One group of researchers[2,8,10,11] found that in multiple extractions the incidence varied from 34 to 85.7 per cent. A second group of investigators[1,3,4,6,12-14] found that a consistently low incidence of bacteremia occurred when only one or two teeth were removed. The author's findings confirm the conclusions of the second group of investigators.

■ *Summary*

Epinephrine in concentrations of 1:100,000 as a vasoconstrictor in 2 per cent anesthetic solution does not reduce the incidence of bacteremia after tooth extraction.

In this study, the incidence of bacteremia increased when teeth were removed from mouths where a poor oral condition existed.

Study supported in part by a grant from the Novocol Chemical Mfg. Co., Brooklyn, New York.

Condensation of a thesis submitted in partial fulfillment of the requirements for a degree of Master of Science (Oral Surgery) at Ohio State University.

The opinions or assertions contained herein are those of the author and are not to be construed as official or as reflecting the view of the Department of the Air Force or the air service at large.

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■ How Often Are You Ill?

The average American suffers an injury or is ill about two and a half times a year, the National Health Survey shows. The incidence of injury and illness is highest in the youngest age groups and decreases progressively with age. The rates ranged from an average of four illnesses per year among children under five to 1.6 illnesses a person 65 years old and over. Respiratory ailments accounted for 65 per cent of all the illnesses. Respiratory ailments caused an average of seven days of restricted activity per person. The days of restricted activity included 219 million days lost from work, and 196 million days lost from school.—*AMA News, Feb. 9, 1959, p. 6.*

Physical properties of commercial solutions of local anesthetics

■ *Wayne Hiatt,* D.D.S., Columbus, Ohio*

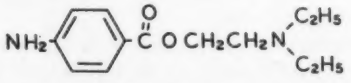
Ten commonly used local anesthetic solutions were studied with special reference to their pH and their osmotic pressures. Little variation in pH was noted with the exception of lidocaine 2 per cent (aqueous) which had a pH of 6.22 compared to the other solutions which varied from 4.03 to 4.61. Since osmotic pressure theoretically should play an important part in the onset of local anesthesia, the melting points of the various solutions were determined. It was found that seven of the solutions were hypertonic, two were hypotonic and one was isotonic.

The literature is vague concerning the physical properties of commercially prepared solutions of local anesthetics. The incidence of initial injection pain, local postoperative sequelae and systemic reactions and questions concerning onset and duration are sufficient stimuli to warrant investigation of the physical properties of commercial local anesthetic solutions. The first section of this paper is a discussion of the pH analysis of ten widely-known commercial anesthetic dental cartridge solutions. Section two is concerned with a comparison of the osmotic pressure effect of the same ten solutions to an isotonic sodium chloride solution.

■ *Chemistry and pH of Commercial Dental Cartridge Solutions*

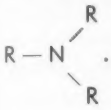
Local anesthetics commonly used today are chemically similar. With the exception of lidocaine, all are primarily esters of benzoic acid with variations in side chains. Lidocaine is an anilide very similar in basic structure to the other local anesthetics, and it follows the same sequence of chemical reactions which occur for any one of the ester group. Therefore, unless stated otherwise, all the chemical reactions in this paper are valid for any of the local anesthetic solutions used in dentistry today.

Local anesthetics are synthetic basic alkaloids which may be represented by the formula for procaine:

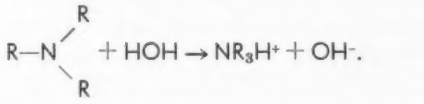


The word "alkaloid" indicates that these agents, because of the tertiary amine group, react as alkalies in chemical reactions. This group is capable of reacting

with water to form a weak base. Local anesthetic agents which are tertiary amines can be represented by the formula



. Nitrogen is capable of having a valence of three or five which can be seen in the following reaction:



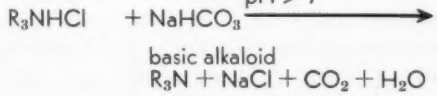
The hydroxy ion OH^- freed by the slight ionization of the reaction allows all local anesthetics to react as alkaline compounds.

The synthetic basic alkaloid compound, represented by R_3N, is only slightly water soluble. It must be converted to a salt form which is water soluble by reaction with an acid such as hydrochloric acid. This is indicated by the following reaction (no. 1):

$$R_3N + HCl \rightarrow R_3NHCl$$

The resulting salt, indicated by R_3NHCl, is water soluble and stable. Commercial solutions are of this nature.

When this solution is injected into body tissues, it will react with tissue fluid as indicated by the following reaction (no. 2):



$$R_3NHCl + NaHCO_3 \rightarrow R_3N + NaCl + CO_2 + H_2O$$

A pH greater than 7 is required to drive this reaction to the right. Tissue fluid normally has a pH of 7.3 or 7.4. The anesthetic potency of the basic alkaloid liberated is approximately six times greater than that of the acid salt.[1] The pH may be decreased to a range of 4 to 6 in areas of inflammation.[2] This interferes with the liberation of the potent basic alkaloid with a resulting inadequate anesthetic effect.

Normally the original basic alkaloid, R_3N, is liberated in the tissue near the nerve trunk. It is only slightly soluble in water but is extremely soluble in lipoids. Since nerve tissue is rich in lipoids, the basic alkaloid is attracted into nerve tissue.

Several physical and chemical reasons for inadequate anesthesia are as follows:

1. The pH of the resultant environment in the region of injection is too low. If the pH is less than 7, reaction no. 2 does not go to completion to liberate the potent lipoid-soluble R_3N. This is often due to inflammation in the region of injection. It may be due also to a commercial acid salt solution whose pH is entirely too low. This situation is not found in present anesthetic solutions.

2. The pH of the resultant environment in the region of injection is too high. If the pH is greater than 8, the alkaloidal base may precipitate and be ineffective. It is highly improbable that the pH of any anesthetic solution is ever this high or that the pH of any healthy patient's tissue fluid ever reaches 8.

3. Excessive dilution occurs with blood and tissue fluid. Assume that an arbitrary unit of a local anesthetic solution deposited an arbitrary unit of distance from the target nerve stops conduction of all impulses. If the solution is deposited two units of distance from the target, the

Table 1 • pH of commercial solutions of local anesthetics

Name	pH
1. Ravocaine HCl 0.4%, Novocain 2%, Neo-Cobefrin 1:20,000	4.28
2. Unacaine Hydrochloride 3.8%, Supranol (epinephrine) 1:60,000	4.53
3. Xylocaine HCl 2% (aqueous)	6.22
4. Xylocaine HCl 2%, Epinephrine 1:100,000	4.23
5. Novocain 2% Solution	4.50
6. Monocaine HCl 2%, Epinephrine 1:50,000	4.22
7. Primacaine HCl 1½%, Epinephrine 1:125,000	4.03
8. Oracaine HCl 2%, Epinephrine 1:50,000	4.61
9. Novocain 2%, Pontocaine HCl 0.15%, Cobefrin 1:10,000	4.46
10. Ravocaine HCl 0.4%, Novocain 2%, Levophed 1:30,000	4.23

amount of solution required to stop all conduction is four times as great, and so forth.

4. Too rapid absorption into systemic circulation occurs. The anesthetic solution is transported into the systemic circulation rapidly if the solution is injected into a highly vascular region. Also, local anesthetic solutions, with the possible exception of lidocaine, are vasodilators. Therefore, a solution such as 2 per cent procaine without a vasoconstrictor is absorbed rapidly.

■ *Methods and Results*

A Beckman glass electrode pH meter Model G was used for the pH determinations. It was standardized with a Coleman certified buffer solution whose pH is predetermined by the manufacturer at 6.00 with an accuracy of ± 0.02. This standardization was then checked by use of a saturated solution of potassium acid tartrate of analytical reagent grade whose known pH is 3.57. A minimum of two determinations was made on a minimum of three different cartridges of each local anesthetic commercial solution. The pH value in Table 1 is the mean of at least six determinations. The variation among the different determinations of the same anesthetic solution was limited to the hundredths decimal in all instances. The instrument was restandardized at various times during the measurements to avoid incorporating an accumulative error. The results are shown in Table 1.

■ *Discussion*

There are many excellent local anesthetic solutions available for dental anesthesia. Many dentists have a personal choice of agent if there is no contraindication for its use on a particular patient. The reason for the personal choice is without doubt due to the satisfactory results obtained by the dentist over a long period. He can also achieve a similar degree of success with some other solutions if they were applied to the same test of time.

The pH determinations were made in order to evaluate what possible effects the solution's pH might have on the various qualities of the different solutions. The variation in pH among the solutions does not appear to be great enough to

have any significance on performance of the solution.

■ *Osmotic Pressure*

Primitive life started in an aqueous environment, and all forms of life today are dependent on the integrity of this fluid environment. In the process of evolution and development, man has become enclosed with a nearly waterproof layer of skin which greatly enhances his activity but burdens him with the necessity of maintaining his body fluids in the correct state. Body water can be divided into two major components called intracellular and extracellular. Intracellular water, which is contained within the individual cell structure, makes up 50 per cent of the body weight. Extracellular water, comprising 25 per cent of body weight, is made up of water found outside cellular walls.

Water distribution in the body is governed by a force known as the osmotic pressure which is equivalent to the hydrostatic pressure necessary to prevent osmosis. This pressure is the result of unequal pressure on two sides of a membrane. Osmosis may be defined as the diffusion of water through a semipermeable membrane to a site of lower water concentration.

If an aqueous solution is separated from a sodium chloride solution by a membrane permeable to both solutions, salt will diffuse into the aqueous solution and water will diffuse into the salt solution until both solutions are of equal concentration.

If a solution of salt is separated from an aqueous solution by a membrane permeable to water but impermeable to salt, then salt bombards the membrane but cannot pass through it, but water passes freely through the membrane from the aqueous side to the saline side. This is in accordance with the law of diffusion: a higher concentration diffuses toward a lower concentration. This water diffusion, which is called osmosis, will continue as long as the water solution is present and until the salt solution is infinitely dilute.

Finally, if a membrane, impermeable to all salts but permeable to water, separates solutions of sodium chloride and potassium chloride of equal concentration, water will diffuse freely in both directions through this membrane at an equal rate. Both solutions have the same osmotic pressure and are known as isotonic solutions. This isotonicity is completely independent of the particular solutes but is dependent on the concentration and ionization of the solutes. Thus the osmotic pressure of a solution depends on the total number of molecules or ions or both present in a given volume of solution.[3]

The osmotic pressure developed by a solution is equivalent to the pressure that the dissolved substance would develop if it were a gas at the same pressure and temperature. One gram molecule of any gas at 760 mm. mercury and 0°C. has a volume of 22.4 liters. Compressed to a volume of 1 liter, it develops a pressure of 22.4 atmospheres at 0°C. On this basis, the following gas laws apply to solutions exerting osmotic pressures:[4]

Avogadro's law: Solutions with the same osmotic pressure at the same temperature contain the same number of particles per unit volume.

Boyle's law: At a constant tempera-

ture the osmotic pressure is proportional to the particle concentration.

Gay-Lussac's law: With a constant particle concentration the osmotic pressure is proportional to the absolute temperature.

Dalton's law: If several substances are dissolved in the same solvent, each one develops osmotic pressure as if it were the only substance dissolved; therefore, the total osmotic pressure is the sum of the osmotic pressures of all of the substances in solution.

The osmotic pressure of a solution may be measured by indirect methods such as melting point, boiling point or vapor pressure. The melting point, or freezing point, method is the method of choice for determining the concentration of a solution containing many different solutes. The melting point of a solution is lower than that of the solvent. The depression of the melting point is proportional to the concentration of the particles in it. The osmotic pressure of the solution can be calculated by measuring this depression in melting point.

Solutions exhibiting the same osmotic pressure are referred to as being "isotonic." When solutions are being compared to a standard solution such as blood or tissue fluid, the terms "hypotonic" indicating lower osmotic pressure and "hypertonic" indicating higher osmotic pressure are employed. The osmotic pressure of whole blood is approximately the same as that of plasma or blood. Human plasma melts at −0.56°C. which corresponds to a 0.3 molar solution, since any nonionizing 1 molar solution melts at −1.86°C. under standard conditions.

A 0.9 per cent sodium chloride solution, which is assumed to be completely ionized (Na^+, Cl^-), is isotonic with blood and tissue fluid. This solution contains 9 Gm. per liter. Thus 9 Gm. of sodium chloride × 2 (number of ionization species) ÷ 58.5 (gram molecular weight) = 0.56 which is equivalent to the ion concentration of blood or tissue fluid.

Commercial local anesthetic solutions contain many constituents. The local anesthetic is present in the form of its hydrochloride salt, for example, procaine hydrochloride. Vasoconstrictors such as epinephrine are present in the majority of commercial solutions. Salts such as $NaHSO_3$ (sodium bisulfite) are added to prevent oxidation of the solution. According to Dalton's law, the total osmotic pressure of a solution is equal to the sum of the constituent pressures. The increase in osmotic pressure of the solution by the addition of inert salts is in direct proportion to the amount of ionization of these salts. Therefore, the concentration or osmotic pressure of a solution can be varied and controlled easily by the amount of inert salts added to the solution.

Local anesthetic solutions should be nearly isotonic with tissue fluid. However, since the volume being injected is relatively small, a slight variation from isotonicity should not be significant. When a hypotonic solution is injected into a region containing nerve tissue, the solution should have a tendency to be attracted into the nerve cells with a higher concentration of ions. Theoretically this should aid in the onset and depth of anesthesia.

Individual cells should exhibit expansion due to accumulation of the hypotonic solution. When a hypertonic solution is injected into the same region,

water from the nerve cells migrates into the region of the anesthetic solution. This could cause a shrinkage or "crenation" of the cellular walls. Crenation is considered as a possible cause of postoperative pain after the injection of hypertonic solutions.

Experiments have been carried out to determine the relation between the osmotic pressure of a solution and the pain associated with the injection of the solution subcutaneously.[5] Pain and the appearance of a wheal at the site of injection were observed when a 0.1 per cent sodium chloride solution was injected. As solutions of increased concentration were injected, the symptoms decreased and were absent at 0.6 per cent sodium chloride concentration. Symptoms remained absent as the concentrations were gradually increased to 2.5 per cent, when pain and wheal formation were again encountered. These results, when considered with the possible advantages of a hypotonic anesthetic solution, would seem to indicate that the optimum osmotic pressure of local anesthetic solutions is in the range equivalent to 0.6 per cent to 0.8 per cent sodium chloride solutions.

■ *Methods*

Melting point determinations on the various solutions were made by using a resistance thermometer calibrated by the National Bureau of Standards. The thermometer indicates an increase in the number of ohms of resistance in its electrical circuit as the temperature of the solution in which it is immersed is increased. This increase in ohms is directly proportional to the increase in temperature of the solution. This thermometer showed a resistance of 25.5860 ohms at 0.00°C. and a resistance of 25.0761 ohms at −5.00°C. Solutions were frozen, and the ohms of resistance at the melting points were recorded.

A sample calculation is as follows:

$$\text{M.P.} = -5.00^\circ\text{C.} \times \frac{A - X}{A - B}$$

where M.P. is the melting point of the solution, and A is the resistance in ohms indicated by the resistance thermometer when immersed in a solution at 0.00°C. and B is the resistance in ohms indicated by the resistance thermometer when immersed in a solution at −5.00°C. and X is the resistance in ohms indicated by the resistance thermometer when immersed in an anesthetic solution at its melting point.

$$\text{M.P. (Sol. no. 1)} = -5.00^\circ\text{C.} \times \frac{25.5860 - 25.5362}{25.5860 - 25.0761} = -0.49^\circ\text{C.}$$

The melting points of anesthetic solutions mean very little in themselves but they can be related to the melting points of known concentrations of sodium chloride. The melting point of a 0.90 per cent solution of sodium chloride was determined to be −0.49°C. This was chosen since it is considered to be isotonic with tissue fluid. With these data the melting points of the various anesthetic solutions may be converted to indicate the concentration of a sodium chloride solution of corresponding concentration or osmotic pressure.

A sample calculation is as follows:

$$X = \frac{T_2 \times 0.90\%\ \text{NaCl}}{T_1}$$

Table 2 • Melting point of local anesthetic solutions and concentration of sodium chloride solution of corresponding osmotic pressure

Name	Melting point (in °C.)	Equivalent in osmotic pressure to NaCl solution of the following concentration (in %)
0.90% NaCl	−0.49	
1. Ravocaine HCl 0.4%, Novocain 2%, Neo-Cobefrin 1:20,000	−0.49	0.90
2. Unacaine Hydrochloride 3.8%, Supranol 1:60,000	−0.66	1.21
3. Xylocaine HCl 2% (aqueous)	−0.60	1.10
4. Xylocaine HCl 2%, Epinephrine 1:100,000	−0.64	1.17
5. Novocain 2% Solution	−0.54	0.99
6. Monocaine HCl 2%, Epinephrine 1:50,000	−0.48	0.88
7. Primacaine HCl 1½%, Epinephrine 1:125,000	−0.64	1.17
8. Oracaine HCl 2%, Epinephrine 1:50,000	−0.69	1.26
9. Novocain 2%, Pontocaine HCl 0.15%, Cobefrin 1:10,000	−0.54	0.99
10. Ravocaine HCl 0.4%, Novocain 2%, Levophed 1:30,000	−0.48	0.88

where X is the concentration of the sodium chloride solution corresponding in osmotic pressure to that of the anesthetic solution and T_1 is the melting point of 0.90 per cent sodium chloride solution and T_2 is the melting point of the anesthetic solution.

$$\text{(Anesthetic solution no. 3)} = \frac{-0.60°\text{C.} \times 0.90\%\ \text{NaCl}}{-0.49°\text{C.}} = 1.10\%\ \text{NaCl}$$

The osmotic pressure of anesthetic solution no. 3 is equivalent to that of a 1.10 per cent sodium chloride solution (Table 2). This solution is slightly hypertonic when compared to tissue fluid.

■ *Discussion*

All local anesthetic solutions used in this study contained inert salts whose only purpose is to increase the solution concentration or osmotic pressure into a range where it is nearly isotonic with tissue fluids. According to the data obtained in this study, several solutions have more inert salts added than would be required to provide isotonicity. However, the degree of hypertonicity does not seem to be significant in view of the relatively small amount of solution injected at any one time.

■ *Summary*

The pH of ten different local anesthetic commercial solutions was determined with an accuracy of −0.02. There was very little variation in pH of the same local anesthetic solution when determinations were made from cartridges obtained from different stock containers. Lidocaine 2 per cent (aqueous) with a pH of 6.22 is considerably less acid than the other solutions tested. The pH range of all other solutions tested was between 4.03 and 4.61.

The melting points of ten different local anesthetic commercial solutions were determined with an accuracy to two decimals. These melting points were compared to that of an isotonic 0.90 per cent sodium chloride solution. By mathematical calculation, the sodium chloride solution of equivalent osmotic pressure for each anesthetic solution was determined.

One anesthetic solution was isotonic with tissue fluid and two other anesthetic solutions were very slightly hypotonic. The remaining seven solutions were hypertonic.

Paper presented for credit, graduate course in dentistry, Ohio State University.

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Postoperative tracheal oxygen at the end of expiration

■ *John A. Zink,* D.D.S., Columbus, Ohio*

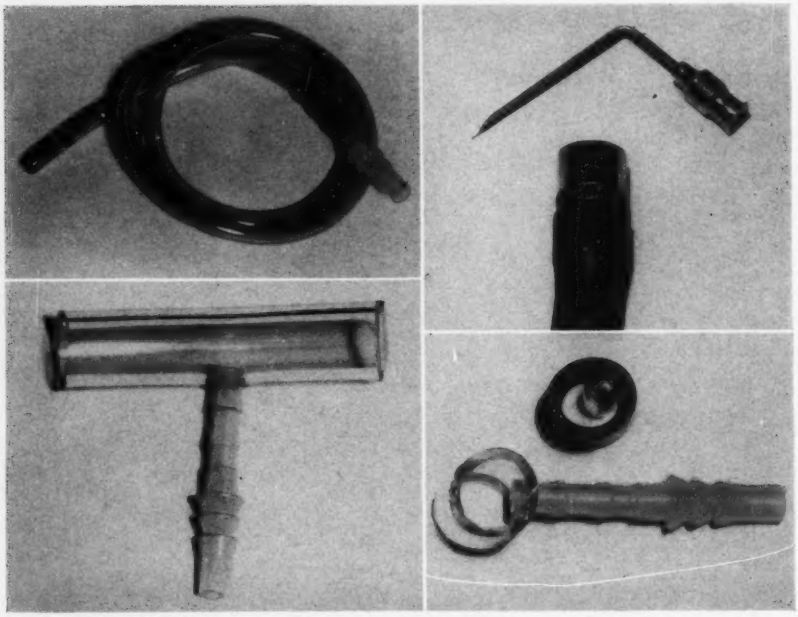
By measuring tracheal oxygen concentration at the end of expiration, three methods of oxygen insufflation through endotracheal tubes were investigated. Although differences in tracheal oxygen found among the three methods did not appear to be of practical significance, the greatest oxygen concentration was obtained with the T-tube technic. Additional work is being planned on this problem correlating a variety of factors which influence tracheal oxygen and consequently reflect alveolar oxygen concentration.

Tracheal oxygen concentration at the end of expiration is a reflection of alveolar oxygen concentration. These concentrations of oxygen are important to the patient's welfare and recovery. The efficiency of methods of oxygen administration through endotracheal tubes during the postoperative recovery period was studied.

■ *Methods*

Twenty-five patients were selected without consideration of the type of surgery performed, the anesthetic agents or technics used, or the duration of anesthesia. Patients were 14 to 62 years of age. The average age was 43 years.

A 5 liter flow of oxygen was introduced into the endotracheal tube by three different methods:



Above left: Size 14 French oxygen catheter used for insufflation. Above right: Fifteen gauge needle used to direct oxygen for insufflation. Below left: T-tube consisting of size 14 French oxygen catheter inserted into side of size 36 French plastic tube. Below right: View demonstrating differences in functional cross-sectional area of T-tube and size 14 French oxygen catheter inside endotracheal tube with same diameter

1. A size 14 French oxygen catheter was inserted 3 inches into the endotracheal tube (see the illustration, above left).

2. A 15 gauge needle directed the oxygen into the endotracheal tube (illustration, above right).

3. A size 14 French oxygen catheter was inserted through the side of a size 36 French plastic tube. The plastic tube was 2 inches long and was open at both ends. The catheter was attached at the middle of the tube. This device was called the T-tube (see illustration, below left).

Oxygen was allowed to flow for five minutes through each device before each sample of tracheal air was taken. The fourth sample of tracheal air was taken after the patient had breathed room air for five minutes after oxygen was discontinued. This sample was used as a control. The respiratory tidal volume was measured with a ventilometer before each sample was collected. The degree of postoperative narcosis is influenced by: age and physical condition of the patient; response to stress from the surgical procedure; anesthetic technics and drugs used, and duration of anesthesia. Respiratory minute volume is influenced by postoperative narcosis. This reading remained nearly constant for each patient.

The air samples were obtained with oil-sealed, 20 cc. syringes. Each syringe had a two way stop cock and a size 14 French oxygen catheter attached. The catheter was inserted through the endotracheal tube and extended into the trachea. Each syringe was filled with air at the end of expiration.

Tracheal air samples were collected in numbered syringes. The method of oxygen administration and the time the sample was collected were recorded. The tracheal air samples were analyzed for percentage of oxygen using the Scholander gas analyzer, and the results were recorded. The technician did not know the identity of the samples except by number.

■ *Results*

The average tracheal air oxygen of all samples collected was as follows: for method 1, 37 per cent (range 22 to 44); for method 2, 35 per cent (range 24 to 42), and for method 3, 42 per cent (range 25 to 59). The average tracheal air oxygen after breathing room air for 5 minutes was 19 per cent (with a range of 15.1 to 21).

■ *Discussion*

Three methods of oxygen insufflation through endotracheal tubes were used. Accurate analysis of the percentage of oxygen was made of tracheal air samples taken at the end of expiration. Variations in the functional cross-sectional area of the airway change the inertia of respired gases. Resistance to flow of a gas through a tube is inversely proportional to the square of the diameter of the tube. Under the conditions of this investigation, the "skin effect" does not affect noticeably the resistance to flow, and remains relatively constant. Reduction in the functional cross-section area of the endotracheal tube increases the frictional resistance to flow of inspired and expired air. An oxygen catheter or needle or both in the endotracheal tube will produce this effect. The T-tube is designed to insufflate oxygen without reducing the functional cross-sectional area of the endotracheal tube (see illustration, below right). The T-tube is the most efficient of the methods of oxygen insufflation studied.

■ *Summary*

Oxygen insufflation by three technics into endotracheal tubes was used during the postoperative recovery period of 25 patients.

Differences in tracheal oxygen found among the three methods of oxygen insufflation did not appear to be of practical significance. The greatest tracheal oxygen concentration was obtained with the T-tube technic.

Tracheal oxygen concentration was lowered significantly when the patient breathed room air. A difference between average oxygen concentrations in these samples and in normal average alveolar air represents an influence of either previously insufflated oxygen or aspiration of room air from the trachea.

Additional investigation of postoperative alveolar air oxygen for both outpatients and inpatients is planned. Correlation of type and duration of anesthesia, the surgical procedure, general physical status of the patient, and postoperative vital signs will be made.

Paper presented for credit, graduate course in surgery (anesthesia).

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Clinical investigation of three synthetic narcotic drugs: a double blind study

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A double blind study was made to test the analgesic properties of three synthetic narcotic drugs, anileridine hydrochloride, levorphanol tartrate and alphaprodine hydrochloride. In addition, meperidine hydrochloride, codeine and a placebo were used. Ten male patients in good general health were selected for the study. The anterior maxillary and mandibular teeth were stimulated with the Burton Vitalometer to determine the threshold of pain perception. Anileridine hydrochloride produced some effect on the vital signs, but there were no substantial changes with alphaprodine hydrochloride; there was rather severe depressions when levorphanol tartrate was administered. Nausea was produced by all three drugs. Anileridine hydrochloride and alphaprodine hydrochloride raised the pain threshold, whereas levorphanol tartrate did not.

Reports that anileridine hydrochloride (ethyl 1-(4-aminophenethyl)-4-phenylisonipecotate dihydrochloride), levorphanol tartrate (levo-3-hydroxy-N-methylmorphinan tartrate dihydrate) and alphaprodine hydrochloride (1,3-dimethyl-4-phenyl-4-piperidyl propionate hydrochloride) were effective analgesics suggested an investigation to study their ability to raise the threshold of the pain receptors of the tooth pulp. Anileridine hydrochloride was reported to be two and a half times as potent as meperidine hydrochloride, although duration of action was slightly less.[1,2] Side reactions were similar to those of meperidine hydrochloride except that anileridine hydrochloride produced a more unpleasant feeling, less drowsiness, and less depression of respiration and blood pressure.

Alphaprodine hydrochloride was compared with other narcotics, and the onset of action was reported to be five to 15 minutes, and duration was approximately two hours.[3,4] Respiratory depression was less than with other narcotics.[5] Diaphoresis, dizziness and, rarely, nausea and emesis were reported as side effects.[6] Because of the short duration of action, alphaprodine hydrochloride had greater flexibility in repeated doses.[7-10]

Levorphanol tartrate was comparable to morphine sulfate in analgesic potency and duration, and was effective when the drug was given orally.[11] Side effects were observed more frequently in ambulatory patients.

■ *Methods*

Ten male patients selected for this double blind study had good general health and above average intelligence and reliability. Their ages ranged from 23 to

34 years. All agents used were identified by a letter known only to the author's adviser, and were supplied at random for use in the project. The identity of all agents was unknown to the investigator and the patient. Each patient participated in this study on eight different days. The patients were not restricted in any way as to diet or activity prior to appointments but were required to remain quiet during the test period. They were permitted to stand whenever they desired but spent most of the experimental period in the dental chair. Blood pressure, pulse, respiratory rate and size of pupils were recorded before premedication, 15 minutes after premedication, and every 30 minutes thereafter for three hours. Pulse pressure remained nearly constant in all patients, so only systolic pressure is reported in this article. Subjective and objective symptoms were recorded.

The anterior teeth of the maxilla and the mandible were stimulated with the Burton Vitalometer at 30 minute and 90 minute intervals when the drugs were administered parenterally, and at 60 minute and 120 minute intervals if they were administered orally. Changes in threshold of pain perception were recorded by measuring responses to high frequency waves which induce pain. The teeth to be stimulated were dried and the stimulating electrode moistened and placed against the labial surface of the junction of the middle and cervical third of the crown. The percentage of increase in threshold of pain perception was found by using the formula:

$$\frac{\text{Mean control value minus mean test value} \times 100}{\text{mean control value}} = \% \text{ threshold change}$$

■ *Results*

ANILERIDINE HYDROCHLORIDE—Anileridine hydrochloride administered subcutaneously produced onset of symptoms in five to 15 minutes in all patients, and the duration of subjective symptoms was from 90 to 120 minutes (Table 1). Anileridine hydrochloride administered orally produced only sedation in three patients, with a variable onset of 60 to 240 minutes (Table 2). Elevation in the threshold of pain from parenterally administered anileridine hydrochloride was moderate in eight patients and there was minimal change in two patients. No change in pain threshold was observed in the seven patients given anileridine hydrochloride orally.

The effect on systolic blood pressure was extremely variable and was not predictable in relation to dosage. Subcutaneous administration of anileridine hydrochloride produced both a rise and a fall in systolic blood pressure in two patients, whereas systolic pressure decreased only in four patients. Orally administered anileridine hydrochloride produced a decrease of systolic pressure of 5 to 15 mm. of mercury in seven patients and no change in two patients.

Side effects from subcutaneous administration of anileridine hydrochloride were more frequent than previously reported.[1,2] The drug produced nausea in four of eight patients, and emesis in two of these patients. Anileridine hydrochloride administered subcutaneously produced an unpleasant feeling in four pa-

tients even when nausea was not present. No side effects were observed from oral administration of anileridine hydrochloride.

LEVORPHANOL TARTRATE—Eight patients were given levorphanol tartrate, 4 mg. orally, and no symptoms were observed. The onset of subjective symptoms, such as mild drowsiness, was extremely variable and changes in vital signs were not severe. Two patients reported that they were constipated the following day. There were no significant elevations in the pain threshold in the first two hours.

When levorphanol tartrate was administered subcutaneously, the response was more intense. Five patients received 4 mg. and three patients received 2 mg. All patients were put under sedation. Nausea was felt by 75 per cent of the patients and was accompanied by emesis in all but one patient. Symptoms were first noticed 10 to 15 minutes after administration of the drug; 62 per cent of the patients had itching of the nose, chest and pudendal areas and dryness of the mucous membranes. The systolic blood pressure changes ranged from no change to 30 mm. of mercury decrease, with an average decrease of 15 mm. When the dose was 4 mg., the effects on vital signs were much greater, and severe decreases were seen in the pulse rate of two of the patients. The pulse of one patient was 48, a decrease of 25 beats per minute and the pulse rate of the second patient was 54, a decrease of 30 beats per minute. These patients were more intensely ill and noticeably sedated than the others. Their pupils were dilated and reacted slowly to light. Respiratory effects were variable, and although depression of respiratory rate was seen in some patients,

Table 1 • Observations on eight patients given anileridine hydrochloride subcutaneously

Mg. per kg.	% Threshold elevation		Systolic blood pressure change	Change in pulse rate	Change in respiratory rate	Side reactions
	½ hr.	1½ hr.				
0.63*	3.5	0.0	+10 to −10	—	—	Sedation (2 hr.)
0.7	14.3	10.7	0	—	−4	Nausea (1 hr.) emesis (3 hr.) sedation (2 hr.)
0.55	6.0	6.0	−5	−6	−4	Nausea (1 hr.) sedation (1½ hr.)
0.63	13.2	9.0	−5	−6	−4	Nausea (45 min.) sedation (2 hr.)
1.22	17.0	28.8	+20 to −5	+20	−4	Sedation (1½ hr.)
1.2	33.3	21.7	−15	−12	−8	Nausea with emesis (3 hr.) sedation (2 hr.)
0.67	18.4	12.6	−10	−6	—	Sedation (2 hr.)
0.63	15.2	12.6	0	−6	—	Sedation (1½ hr.)

*Patients are reported in same order in which they received the drug. Similar charting of results of tests with the drugs was made.

Table 2 • Observations on nine patients receiving anileridine hydrochloride orally

Mg. per kg.	% Threshold elevation		Systolic blood pressure change	Change in pulse rate	Change in respiratory rate	Side reactions
	1 hr.	1½ hr.				
1.0	0.0	18.0	−10	—	−4	———
1.0	0.0	13.3	0	—	0−4	———
0.73	8.3	6.0	−10	—	−4	———
0.71	11.6	4.3	−15	−12	+4	Sedation
0.75	0.0	0.0	−10	−12	−4	———
0.75	0.0	0.0	−10	−8	−4	Sedation
0.80	0.0	0.0	−5	—	—	———
0.80	0.0	0.0	−10	−6	0−4	———
0.66	0.0	0.0	0	−12	—	Sedation

it was not predictable. The effect on threshold of pain perception was minimal.

ALPHAPRODINE HYDROCHLORIDE—Alphaprodine hydrochloride was used subcutaneously in nine patients. The subjective symptoms began in from three to seven minutes. The first symptoms were dizziness, sedation, a sensation of weakness and mild euphoria. Fifteen minutes after the injection, there was an onset of mild, itchy sensations (nose, chest and pudendal areas) in all of the patients; the duration of these sensations was 30 to 120 minutes. The respiratory rate was usually decreased by four to six breaths per minute, and this reduction in rate lasted from 90 to 120 minutes. If there was no reduction in respiratory rate, there was a decrease in tidal volume, and one patient developed an irregular rhythm. Changes in amplitude and rhythm lasted approximately 30 minutes. The systolic blood pressure decreased as much as 15 mm. of mercury with an average drop of 5 mm. of mercury. This variable does not appear to be significant because normal readings were obtained on these patients at various times throughout the three hour testing period. The pulse rate decreased 12 to 18 beats per minute in all patients. The quality of the pulse remained normal and regular.

The side effects noted were of great interest. Seven of the nine subjects were nauseated at one time or another, with the greatest incidence of nausea occurring after the patients left the examining area. Five of these seven vomited and this occurred with surprising regularity at about eight hours after they had received the drug. The incidence of nausea and vomiting was unrelated to dosage. All patients were well sedated and the duration of sedation was from 90 to 120 minutes. At dosages over 1 mg. per kilogram there was noticeable muscular incoordination and decreased visual accommodation. The sensations of itching and dryness of the mucous membranes were felt by all patients.

The drug not only elevated the pain threshold substantially but each patient, without exception, made the statement

that the pulp stimulation was painful but that he did not mind the pain. They believed that the intensity of the stimulus could be increased and they could tolerate it.

MEPERIDINE HYDROCHLORIDE—Meperidine hydrochloride administered subcutaneously produced onset of symptoms in five to 10 minutes, and duration was from 120 to 180 minutes. In the patients receiving this drug, no untoward side effects were seen or reported. Dosage of 1 mg. per kilogram or more produced good sedation and some incoordination of movements. Dryness of the mucous membranes was seen in all patients. Vital signs were mildly depressed. The pulse rate decreased 12 to 18 beats per minute in four of five patients. The change in threshold of pain perception was variable in the first 30 minutes and uniformly small at the last reading.

CODEINE—Codeine was given orally in doses of one grain (five patients) and ¾ grain (seven patients). Codeine has been reported to have a slight effect on the tooth pulp pain threshold.[12] In this study, however, codeine produced no such effect. There were no appreciable changes noted in the vital signs of the majority of patients, and side effects were absent in one patient who was slightly sedated.

PLACEBO — Placebos were administered orally and parenterally during this double blind investigation. Observations made and results obtained with placebo tablets were interesting. Changes in vital signs were variable and blood pressure readings in millimeters of mercury ranged from increases of ten to decreases of ten. The pulse rate per minute usually decreased six but an occasional increase of six to 18 was seen. The respiratory rate was less variable and usually no change was noted. A change in pain threshold was seen in 33 per cent of those tested and ranged from 6 per cent to 15 per cent. If the patient said that he felt drowsy or sedated with a placebo, he usually would have an increase in pain threshold.

The parenterally administered placebo used was sterile water for injection, and in every instance the patient remarked that there was pain in the area of injection that lasted about 30 minutes. Eight patients of nine tested stated that they were sedated, and appeared to be so to the observer. Also, with the exception of one patient, there was a decrease in the vital signs. The blood pressure in millimeters of mercury varied from an increase of ten to a decrease of 20. Pulse rate decrease was from six to 18 per minute. The respiratory rate per minute was decreased two to four respirations. A constriction of the pupils was recorded in many of the placebo testings.

■ *Discussion*

The type of sensory perception that is found in the tooth pulp is one of deep and intense pain.[13] It is similar in nature to sensations that are derived from the periosteum of bone and the cornea of the eye. Therefore, one would expect that to be effective in increasing tooth pain threshold, any analgesic agent or anesthetic agent would have to exert profound influence on sensory nerve conduction or central perception areas. It is important

that the threshold of pain perception rather than the threshold of pain reaction is used when evaluation is made of the changes in pain threshold of the tooth pulp.[14] The problems involved in evaluating analgesic agents with regard to threshold variation in the experimentally produced pain situation have been discussed in recent literature.[15,16]

Analgesics were given to patients who had no pain and knew that they were going to be stimulated to produce pain, an important factor to consider when evaluating the responses obtained. Narcotics produce more unpleasant side effects on patients who are not suffering pain or discomfort.[17] This is also true of the ambulatory patient as compared to the bed-confined patient.

The analgesic or narcotic agent best suited to the needs of the dental practitioner should have certain attributes that might not be necessary or required for other situations: a potent analgesic effect for elevating pain threshold of the tooth pulp tissues; a short duration of sedation or cortical depressant action; lack of side effects that would produce symptoms of the nature that make the patient unable to resume his normal habits after leaving the dental office; a wide margin of safety in systemic effects so that the poor-risk patient could also benefit from its use.

Anileridine hydrochloride produced an analgesia of less intensity than alphaprodine hydrochloride; however, the mean level of analgesia produced was greater than that by meperidine hydrochloride. The duration of sedation by anileridine hydrochloride was a little longer and the sedation was of less depth than by the other drug. It did not produce any pleasant sensations. The effect on vital signs was slight and the incidence of nausea and emesis was less than with alphaprodine hydrochloride. The unpleasant sensations that occurred in all these patients make this drug less desirable than alphaprodine hydrochloride or meperidine hydrochloride for premedication for local anesthesia. These unpleasant sensations should reduce the tendency for addiction. Further study on the use of this drug as an adjunct to general anesthesia may disclose some advantages to be gained by its use.

Levorphanol tartrate did not meet the requirements listed as important for an ideal analgesic and was probably the least desirable agent tested.

Alphaprodine hydrochloride produced the best and most consistent analgesic effect (Tables 3 and 4). There was a moderate degree of sedation evident and a certain feeling of well-being evidenced by all the patients. Vital signs were not changed substantially. The incidence of nausea and subsequent emesis was the most unwelcome effect noted. The high incidence of these side effects might have been decreased if the patients had been subjected to some operative procedure, or if the drug had been used in conjunction with general anesthesia.[18] Increase in pain threshold of the tooth pulp and euphoria from alphaprodine hydrochloride were more satisfactory than the results obtained with meperidine hydrochloride. However, alphaprodine hydrochloride produced nausea in 77 per cent of patients tested, and meperidine hydrochloride caused no nausea.

Every drug given orally produced only a very small degree of analgesia with

Table 3 • Elevation of pain threshold (30 minutes after subcutaneous administration)

Drug	Number of patients in various percentage groups of pain threshold elevation				
	0–10%	11–20%	21–30%	31–40%	41–100%
Alphaprodine hydrochloride	0	3	4	2	0
Anileridine hydrochloride	2	5	0	1	0
Levorphanol tartrate	8	0	0	0	0
Meperidine hydrochloride	1	2	1	0	1
Placebo	7	2	0	0	0

respect to the change in pain threshold of the tooth pulp (Table 5).

There was only a rare instance of sedation noticed and the onset of any subjective effect was unpredictable. It would be interesting to repeat this experiment on patients who had an empty stomach at the time of oral administration of the drug.

In some instances, placebos caused moderate depression of vital signs, sedation and an elevation of pain threshold. Psychic factors influence evaluation of the results of an investigation of this nature. The double blind technic helps prevent false results when psychic influences affect responses.

■ *Conclusions*

1. The tooth pulp is a satisfactory algesimetric site when used in the method described.

2. Analgesic agents which have proved satisfactory for some purposes may not be satisfactory for elevation of threshold of pain sensation in the tooth pulp.

3. Nausea was produced by parenteral use of anileridine hydrochloride (50 per cent of patients), of levorphanol tartrate (62 per cent of patients), and of alphaprodine hydrochloride (77 per cent of patients). Parenteral administration of meperidine hydrochloride and sterile water for injection produced no nausea.

Table 4 • Elevation of pain threshold (60 minutes after subcutaneous administration)

Drug	Number of patients in various percentage groups of pain threshold elevation			
	0–10%	11–20%	21–30%	31–40%
Alphaprodine hydrochloride	3	3	0	3
Anileridine hydrochloride	4	2	2	0
Levorphanol tartrate	8	0	0	0
Meperidine hydrochloride	4	1	0	0
Placebo	9	0	0	0

Table 5 • Elevation of pain threshold (after oral administration)

Drug	Number of patients in various percentage groups of pain threshold elevation			
	60 minutes		120 minutes	
	0–10%	11–20%	0–10%	11–20%
Anileridine hydrochloride	8	1	7	2
Levorphanol tartrate	7	1	8	0
Codeine	12	0	11	1
Placebo	9	2	9	2

4. Anileridine hydrochloride and alphaprodine hydrochloride raised the pain threshold of the tooth pulp more consistently than did meperidine hydrochloride.

5. Levorphanol tartrate did not raise the pain threshold of the tooth pulp, and depressed vital signs severely.

6. There were no changes in pain thresholds or side effects in relation to dosage in patients receiving anileridine hydrochloride and alphaprodine hydrochloride. Fifty per cent of these patients received the recommended dosage and 50 per cent received two times the recommended dosage.

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The alphaprodine hydrochloride (Nisentil Hydrochloride) used in this investigation was supplied by Hoffman-LaRoche, Inc.

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Antihistamines in experimental inflammation

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In order to determine experimentally the efficacy of antihistamines in controlling or preventing oral inflammation, the effect of three well known irritants, including histamine, was evaluated carefully against three common antihistamines in the intact cheek pouch of the Syrian hamster. Although premedication with the antihistamines greatly modified the response to the histamine, the antihistamines had no significant effect on the two other irritants. This strongly suggests that many other factors, both mechanical and biochemical, play a decisive role in inflammation.

Reports have appeared on various clinical and experimental investigations of the effect of antihistaminic agents on inflammation. The present study was undertaken to determine the efficacy of antihistamines in controlling the inflammatory response of oral tissues. Microscopic changes in the tissues of the intact cheek pouch of the Syrian hamster were observed and photographed. The experimental sites then were excised and studied histologically.

■ *Methods*

Eight groups of investigational animals were used. Each group consisted of three adult female Syrian hamsters weighing from 100 to 150 Gm. The antihistamines used were promethazine hydrochloride,[1] tripelennamine hydrochloride,[2] and chlorprophenpyridamine maleate.[3] Experimental animals received 1 mg. of antihistamine intraperitoneally and 1 mg. of antihistamine intramuscularly at the time of anesthetization. Control animals received equivalent volumes of 0.9 per cent sodium chloride solution as a placebo, or no medication.

Under pentobarbital sodium anesthesia, the cheek pouch was everted over a moist chamber observation platform which was fitted to a standard mechanical stage microscope. The temperature of the preparation was maintained at 36 to 38°C. by means of a thermostatically controlled warm-blooded Ringer's solution continuous drip (Fig. 1).

A stabilization period of 30 minutes was allowed before introducing irritation into the cheek pouch. During this period the entire pouch was examined microscopically for any evidence of damage or undue changes caused by the operative preparation. The region for experimentation was chosen from the closed portion of the cheek pouch, which is relatively free of muscle tissue, and at least 1 cm. from any of the fixation pins so as to rule

out any inflammatory process resulting from the pin injury.

The irritants used were as follows:

1. Submucosal injection of 0.01 cc. of a 1/5,000 histamine phosphate solution to produce a response from the direct effects of extracellular histamine. A 5/8 inch 25 gauge needle was introduced remote from the experimental region and advanced between the layers of the cheek pouch. The irritant was deposited directly within the chosen site of observation.

2. A surface burn with a 4 mm. diameter metal rod heated to 90°C. in a water bath was applied to the surface of the cheek pouch for ten seconds to produce a response due only to the products of tissue injury.

3. Submucosal injection of 0.01 cc. of 5 per cent kaolin suspended in 5 per cent gum acacia was used to produce a response resulting from the presence of an agent foreign to the tissue.

Continuous microscopic observation was carried out for 90 minutes. Observable changes in the vascular bed of the experimental region were recorded. Photomicrographs at 35X magnification were taken 15 minutes prior, and immediately prior, to the introduction of the irritant and at 2, 5, 15, 30, 60, and 90 minutes after irritation (Fig. 2, 3, 4). In some instances, photomicrographs at 100X magnification were taken to show reactions in the capillary bed.

Twenty-four hours after inducing the irritation, the animal was again anesthetized and the pouch prepared for microscopic observation using the original fixation points. The original region of experimentation was again observed and photomicrographs taken. The experimental site then was excised and submitted to routine histologic preparation with hematoxylin and eosin stains.

Fig. 1–1, Spencer standard microscope with mechanical stage. 2, Zeiss beam splitter with 35 mm. camera attachment. Leitz 10X periplane ocular lens used in beam splitter. 3, Robot Star Special 35 mm. camera with no lens. (Film used was Kodak Super XX). 4, American Optical 6 volt microscope lamp with variable transformer, and adjustable focus. 5, Reservoir for warm-blooded Ringer's solution with thermostatic temperature control. 6, Lucite plastic animal board with moist chamber observation platform

Changes observed in the vascular bed were graded with the following criteria: (1) vessel size, considering the arterial and venous portions of the vascular bed separately; (2) stasis in any of the arterial or venous vessels or both; (3) edema of the experimental region; (4) petechial hemorrhage formation in the experimental region. The photomicrographs were evaluated in the same manner. The photomicrographic evaluation was recorded as the final value when the results of the two methods differed.

The microscopic slides, after coding and randomization, were evaluated blindly for the degree of inflammatory reaction present on the following criteria: (1) cellular infiltration, number and type(s);

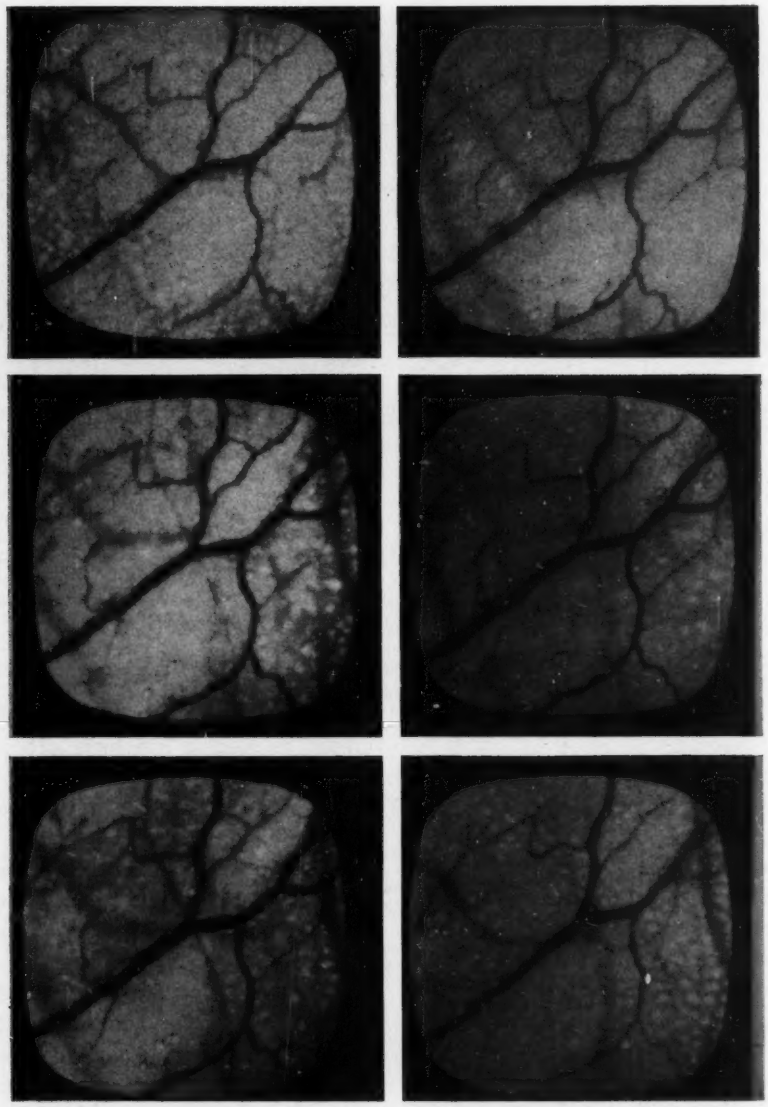

Fig. 2—Photomicrographs of vascular bed after injection of 0.01 cc. histamine phosphate with antihistamine premedication. (Enlarged 2X). Upper left: Normal field after 30 minute stabilization period and immediately prior to injection of histamine. (Magnification 35X). Upper right: Field two minutes after injection. Considerable dilatation and mechanical spreading of tissues. (Magnification 35X). Center left: Fifteen minutes after injection. Considerable dilatation still present. (Magnification 35X). Center right: Thirty minutes after injection. Arterial side normal, venous side moderately dilated. (Magnification 35X). Lower left: Ninety minutes after injection. Moderate dilatation of vascular bed. Note that deeper vessels are more distinct than in the two minute film. (Magnification 35X). Lower right: Twenty-four hours after irritation, and 30 minutes after preparation of pouch for observation. Vessels are of normal caliber. Slight haziness of field as compared to preinjection film, recorded as grade 1 edema. (Magnification 35X)

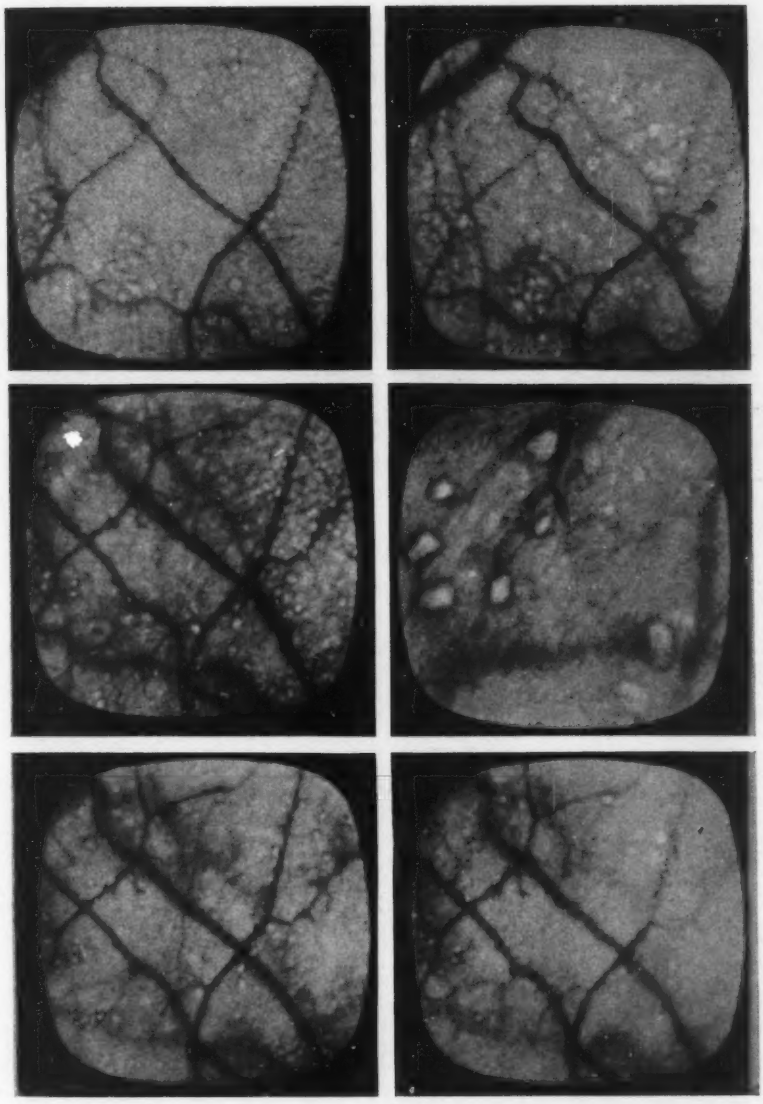

Fig. 3—Photomicrographs of vascular bed after standard burn irritation with antihistamine premedication. (Enlarged 2X). Upper left: Normal field after 30 minute stabilization period and immediately prior to burn irritation. (Magnification 35X). Upper right: Field two minutes after burn irritation. Moderate dilatation of vascular bed. (Magnification 35X). Center left: Field 15 minutes after burn irritation. Marked dilatation and grade 1 edema. (Magnification 35X). Center right: Fifteen minutes after irritation. Widely dilated capillaries and venules. Venule in left lower quadrant of film is in stasis. (Magnification 100X). Lower left: Thirty minutes after irritation. Marked dilatation and progression of edema. (Magnification 35X). Lower right: Ninety minutes after irritation. Grade 2 edema. (Magnification 35X)

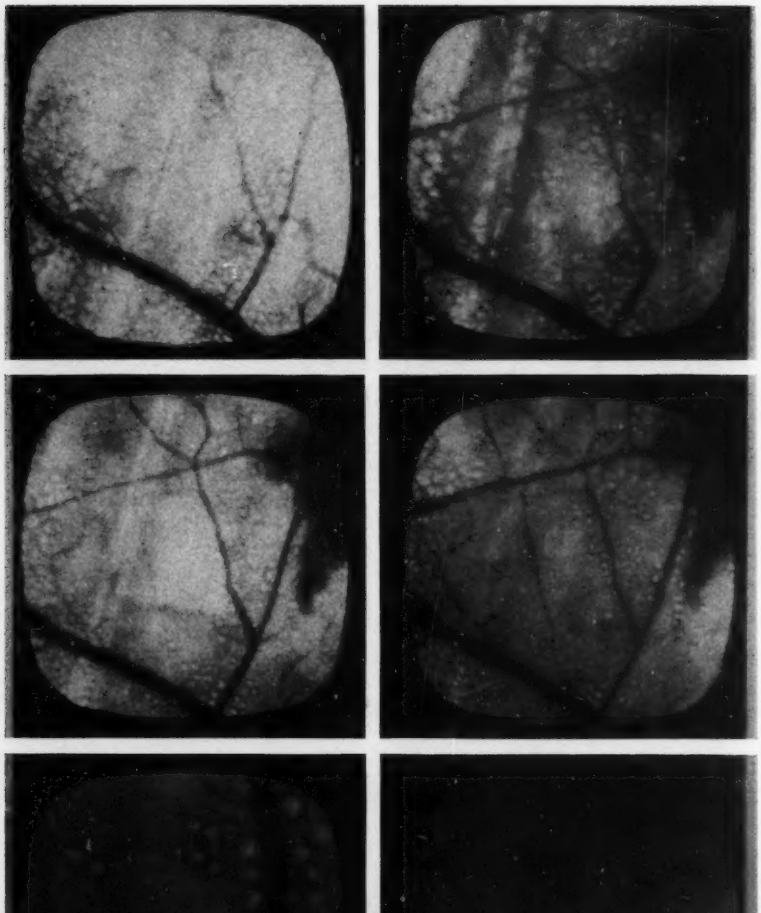

Fig. 4—Photomicrographs of vascular bed after irritation with kaolin-gum acacia injection with antihistamine premedication. (Enlarged 2X). Upper left: Normal field after 30 minute stabilization period and immediately prior to irritation with kaolin-gum acacia injection. (Magnification 35X). Upper right: Field five minutes after irritation with kaolin-gum acacia. Moderate dilatation of vascular bed. (Magnification 35X). Center left: Thirty minutes after irritation. Moderate dilatation, with no great change from five minute film. (Magnification 35X). Center right: Ninety minutes after irritation. Marked dilatation and grade 1 edema. (Magnification 35X). Lower left and right: Twenty-four hours after irritation. Marked dilatation of small bore vessels, grade 2 edema. (Magnification 100X)

(2) vesicle formation; (3) necrosis or abscess formation; (4) interstitial hemorrhage.

The inflammatory responses were graded after tabulation and correlation of all recorded data (see table).

■ *Findings*

Preliminary experiments disclosed no adverse reactions from the operative preparations and procedures or from the antihistaminic agents used.

HISTAMINE PHOSPHATE IRRITATION—All control animals showed a mild to moderate inflammatory response to the locally injected histamine phosphate solution. In the experimental animals protected with the antihistaminic agents used, the response was greatly modified. Two animals showed no significant inflammatory response and two showed only a very mild inflammation (see table).

STANDARD BURN IRRITATION—Two control animals were classified as having a severe inflammatory response. The third showed moderate inflammation of the experimental region. The inflammatory response in the nine experimental animals was classified as very mild in one, moderate in two, and marked to severe in six. All but one of the experimental animals in this group had considerably more inflammation than did the experimental animals of the histamine irritated group.

KAOLIN IN GUM ACACIA IRRITATION—The inflammatory response in the control group was classified as moderate in two animals and severe in one animal. The inflammatory response in the nine experimental animals was classified as marked to severe in eight animals and moderate in one animal. All experimental animals of this group had more marked inflammation than the experimental animals of the histamine group. Eight of nine experimental animals in this group showed a severe response to trauma as compared to six of nine animals in the burn irritated experimental group.

■ *Discussion*

Histamine is rapidly inactivated by (1) the enzyme histaminase, (2) conjugation with acetic acid, and (3) intracellular binding. If histamine is prevented from producing the immediate effects on the vascular bed, it is soon eliminated by these systems and no longer acts as an irritant.

Table • Summary of experiments and their composite evaluations

Irritant	Premedication			
	None	Phenergan	Pyribenzamine	Chlor-Trimeton
Normal saline solution	3 OOO	1 O	1 O	1 O
Histamine phosphate	2 YYY	2 OX	1 X	1 O
Standard burn	3 YZZ	3 XZZ	3 YZZ	3 YZZ
Kaolin-gum acacia	3 YZZ	3 ZZZ	3 YZZ	3 ZZZ

Numbers represent the number of animals in each group.
Symbols represent severity of the inflammatory response for each animal in the group.
O Represents no noticeable inflammatory response (Grade 0).
X Represents very mild inflammatory response (Grade 1).
Y Represents mild to moderate inflammatory response (Grade 2).
Z Represents marked to severe inflammatory response (Grade 3).

Extracellular histamine seems to be more efficiently antagonized by the antihistamines than is intracellular histamine. The antihistamines apparently do not penetrate the cell membranes.

In this study, the effects of locally injected histamine (extracellular) were greatly modified by antihistamine premedication. Histamine was not completely blocked when locally injected but the dilation of the vascular bed was no more severe than that following the submucosal injection of isotonic saline solution. Only by comparison of the "immediate" and "24 hour" photomicrographs was any adverse response detected in the experimental region. Maintenance of relatively "normal" vascular channels was thus accomplished and the release of intravascular components into the adjacent tissues (with subsequent disturbance in metabolism and fluid content) was greatly minimized.

BURN AND KAOLIN-GUM ACACIA IRRITATION—Histamine (H-substance) was less efficiently antagonized if the irritants brought about an intracellular as well as irritants may have released enough hista- extracellular release of histamine (H-substance). The burn and kaolin-gum acacia mine (H-substance) from the cells that its concentration was actually higher than histamine concentration in the locally injected group.

The antihistamines did not alter appreciably the dilatation of the vascular bed after burn or kaolin-gum acacia irritation. Such dilatation would have enhanced the extravasation of the vascular components by a direct effect of the irritants on the vessels, by response through an axon reflex, or by the release of substances other than histamine. Direct injury to the vessel walls by these irritants could result in a severe disturbance of the metabolism and vitality of the endothelium. A loss of capillary semipermeable properties would result. Other substances such as leukotaxine, hyaluronidase, and acetylcholine may have been released within the tissues because of these irritants. The concomitant action of one or several of these agents could not be excluded.

It seems that little or no benefit is derived from antihistamines in relation to that part of the immediate response to injury which may be the result of direct alteration of the vascular walls or which may be due to substances other than histamine (H-substance).

■ *"Secondary Histamine Release"*

If the response which is not antagonized by the antihistamines is severe enough in itself to lead to the formation of edema, this edema in turn could alter the fluid and gaseous exchange of the neighboring tissues. The resultant hypoxia and increase in local metabolites could bring about the release of additional H-substance. Thus a self-propagating process would occur limited only by the tissues' susceptibility to edema, anoxia, and metabolites.

A real difference in the type of injury produced by these irritants over that produced by histamine phosphate injection is quite probable. Although the application of the burn irritation was an acute insult to the tissue and undoubtedly brought about histamine release, the products of tissue breakdown subsequent to

the burn injury represent a source of chronic irritation. The continued presence of a foreign substance in the kaolin-gum acacia irritation may serve as a chronic irritant also. This chronic irritation could have continued to cause vascular dilatation or the release of histamine or other substances.

Although the experimental inflammation in this study was not altered significantly by the antihistamines as used, the region involved was subjected to direct injury only, and the antihistamines were not continued after the injury. Investigation of larger portions of tissue and of maintained antihistamine levels may produce valuable information in this respect.

■ *Conclusions*

1. Premedication with the antihistamines used in this study greatly modified the response to locally injected histamine phosphate solution.

2. Premedication with these drugs did not alter significantly the response to burn irritation or to the irritation produced by local injections of kaolin suspended in gum-acacia.

3. Burn and kaolin-gum acacia irritation have "chronic" irritating factors, whereas locally injected histamine is a "short-lived irritant." Theoretical possibilities for the lack of protection afforded in the burn and kaolin-gum acacia irritation have been discussed.

4. This study does not preclude the possibility that the over-all process of wound healing (tissue repair) might be influenced by antihistamine therapy.—*Toledo Medical Building.*

Condensation of a thesis submitted in partial fulfillment of the requirements for a degree of Master of Science (Oral Surgery) at Ohio State University, 1956.

*Former resident in oral surgery, Ohio State University.

1. Promethazine hydrochloride (Pherergan) supplied for this study by Wyeth Laboratories, Philadelphia.

2. Tripelennamine hydrochloride (Pyribenzamine), Ciba Pharmaceutical Products, Inc., Summit, N. J.

3. Chlorprophenpyridamine maleate (Chlortrimeton). Schering Corporation, Bloomfield, N. J.

■ Teeth Eruption and the Age of Fossils

The practice of dating fossils by studying the sequence of tooth eruption is erroneous. The sequence of tooth eruption in the skulls of fossils has been used in the past to measure the biologic distance between early and recent man. A study of present-day children, however, has revealed that the course of tooth development and eruption is a "variable" phenomenon because the growth period of teeth may be influenced by numerous factors which may reverse the order of tooth development again and again. A tooth eruption sequence, thought to be a unique characteristic of fossil man, was recently found in 16 per cent of Finnish school children and had been reported 50 years ago in children of the Apache and the Pima tribes. No essential difference between the tooth eruption sequences of the permanent teeth in prehistoric and modern man has yet been determined. Attempts to use such an eruption sequence for biologic dating are "fraught with danger," even assuming that a correct interpretation of the anthropologic age can be made.—*Stanley M. Garn and Dalevi Koski, Nature, 1958.*

Functions of a dental clinic in a tuberculosis hospital

■ *John L. Miller,* D.D.S., and Dorothy McGrath,† R.N., Columbus, Ohio*

Dental care for tuberculosis patients as carried out at the Ohio Tuberculosis Hospital is described. This program assures adequate dental care for the patients admitted to the hospital, as well as education of dental students and hygienists. An adequate dietary intake is important to the tuberculosis patient, and can be attained only if the patient has good dental function. Aseptic clinical technic is taught to the dental student and hygienists, thus insuring against the spread of acid-fast organisms to the dental operating team, or to other patients seen in the dental clinic.

The dental health program at the Ohio Tuberculosis Hospital has two objectives: adequate oral health of the patients and education of dental students and hygienists.

The primary responsibility is dental care of patients admitted to the hospital. Body defenses can be concentrated on primary illness if other areas of infection are removed. A balanced diet is important and can be attained only if the patient has good function with natural or artificial teeth.

The Ohio Tuberculosis Hospital is a teaching hospital, and an additional responsibility to education is undertaken. The dental intern completes postgraduate and basic science training. The dentist and the nursing supervisor train and supervise dental students and dental hygienists to use a definite aseptic clinical technic.

■ *Aseptic Technic*

Ninety-eight per cent of the tuberculosis cases are pulmonary, and the tubercle bacilli are present in the saliva of patients who have a positive sputum.[1] The bacillus is a non-spore-forming rod which contains an unusually large amount of lipoid material. Comparatively easy to destroy with heat, it resists chemical disinfection and drying. The bacillus is nonmotile and is transmitted by direct contact or carried as droplets or droplet nuclei in air currents. The aseptic technic at this hospital has been developed to protect both patients and personnel from unnecessary exposure. All employees have routine periodic tuberculin skin tests and chest roentgenograms. BCG vaccine is made available to those

persons who have a negative result to the skin test.

Patients are given sputum tissues and moistureproof bags before they are taken to the dental clinic. Hospital protocol, taught in patient education classes, requires that they cover their cough with a tissue which is placed in the bag.[2] En route to the clinic, the patients use their own separate elevator and must be accompanied by an attendant.

Important reasons for careful selection of dental clinic rooms are: to provide protection of hospital personnel from tuberculosis; to protect the patients from re-infection, and to provide adequate space for student teaching. The rooms must have good ventilation, adequate natural and artificial lighting, and a sink. A small boiling sterilizer and an alcohol soak-pan should be within the room or in the immediate vicinity. The charts, clinic records and films are never used in an area where they might become contaminated.

Clean-up procedure between patients is effective but not time consuming. Paper covers are used on the bracket table; they are discarded after each patient. The saliva ejector, forceps and other boilable instruments are washed with soap and water and boiled for at least ten minutes. Mirrors and electrical attachments which cannot be boiled must be washed thoroughly with soap and water, dried, and soaked in alcohol 70 per cent for ten minutes. When the dentist is through seeing patients, the entire room is cleaned and then aired.

Special apparel is used at the Ohio Tuberculosis Hospital for protection of personnel (Fig. 1). The dentist removes his street clothes and wears a surgeon's scrub suit, a long-sleeved surgical gown,

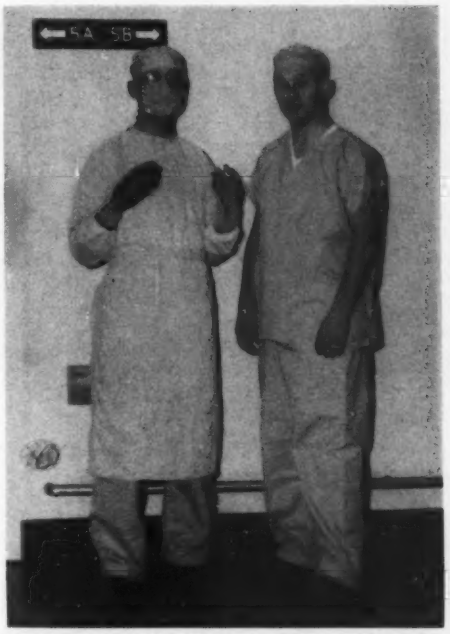

Fig. 1—Scrub suits and surgical gowns worn by dentist for proper aseptic technic in tuberculosis hospital

a surgical cap and an eight-ply gauze mask. The mask must be changed every hour, or more often if it becomes moist. Rubber gloves are worn and changed between patients. The gloves are not worn for sterile technic but to protect the dentist. A quick change of gloves eliminates lengthy scrubs between patients. Glasses are recommended for the dentist to protect his eyes from flying particles. Hospital personnel wipe their shoes clean before leaving the area.

An assistant obtains supplies and instruments while the dentist is working with a patient. His hands become contaminated, and he would need to change gloves or wash thoroughly before opening

Fig. 2—Dental hygienist instructing patient on proper brushing procedure

"clean" cabinets and drawers. The assistant is a nurse aide trained by the dentist. She makes appointments, transports patients, and prepares equipment and the work area. The assistant wears a hospital uniform and uses the regular nursing gown, cap and mask.

■ *Diagnosis and Treatment Plan*

Full mouth dental roentgenograms are requested routinely. Radiation effect from roentgen rays needed to obtain dental roentgenograms is not harmful to the patient if the amount of radiation is kept within average limits.[3]

Healing after oral surgical procedures is slow in debilitated tuberculosis patients because the body's defenses already are under stress. More postoperative complications than usual are expected after dental extractions and other oral surgical procedures. Preoperative and postoperative treatment plans are used to reduce complications. The patients are asked to brush their teeth and to use an antibacterial mouthwash before going to the clinic. An ice bag is applied immediately on the face over the operative site if the patient has had multiple extractions. A dental soft diet is taken until regular food can be tolerated. A warm saline mouthwash is used after meals. Alternate technic and drugs are used for wounds that do not respond to the routine treatment. Delayed healing results in a longer waiting period from the time of multiple extractions until impressions are taken for dentures. Four to six months of healing after oral surgery often are required before final impressions are made.

Many patients are severely debilitated. The dentist limits treatment to fit the ability of the patient to stand stress. The duration of the dental appointment is made as brief as possible since these patients are restless and tire easily. Dental care is restricted to essentials. Inlays, crowns, bridges and partial dentures are not provided in the dental service.

The psychological status of the patient in the tuberculosis hospital is considered in the treatment plan. The patients have already been involved in many therapeutic procedures and usually are not too apprehensive. Premedication with sedatives or tranquilizers is used if needed.

■ *Professional Cooperation*

There must be close cooperation among the various professions for an adequate dental health plan. The dentist at the Ohio Tuberculosis Hospital consults with the resident physician in charge of the patient. This assistance is important, since the individual's general condition must be considered before an extensive dental procedure is performed.

Equally important in the plan is the

information obtained from the head nurse. At each nursing station data are made available about the patient's general condition, therapy and progress.

When major oral surgery is required, it is carried out by a staff oral surgeon and the dental intern, with the assistance of a registered nurse.

The program also includes cooperation with the social service department. This group works out a payment plan for dental prosthetic service for those patients who are unable to provide the minimal cost of the dentures.

The teaching program requires close supervision of students. Dental students and oral hygienists use the aseptic technic when working in the clinic (Fig. 2).

■ *Summary*

1. The dental department at Ohio Tuberculosis Hospital provides essential dental health for the patients.

2. The dental intern learns advanced technics in dental health care. He completes postgraduate basic science courses.

3. Dental students and dental hygienists are assigned for clinic duty in the hospital. The scope of dental education is extended through this valuable teaching aid.

4. The physician house-staff assists the dental intern in patient evaluation and treatment planning. The dental intern teaches the medical personnel the needs and values of dental services for the patient.

5. Cooperation among the dental intern, physician house-staff, dentist on the general dental staff, dentist on the oral surgery staff, and active medical and surgical staffs provide better patient services and interprofessional understanding.

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*Formerly, dental intern, Ohio Tuberculosis Hospital; at present, assistant resident in oral surgery, University Hospital, Ohio State University Health Center.

†Nursing supervisor, Ohio Tuberculosis Hospital.

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■ ANGER

In a controversy the instant we feel angry we have already ceased striving for the truth, and have begun striving for ourselves. When we are wrong and won't admit it, we always get angry.—*Thomas Carlyle.*

A review of hospital dental services and the dental service of the Ohio Tuberculosis Hospital

■ *Richard O. Dagefoerde,* D.D.S., Toledo, Ohio*

Within the recent past, there has been an increasing interest in the development of dentistry as a hospital service to conform to the concept of total treatment planning. The scope of the hospital dental service offered depends on the needs of the individual institution. The organization of the dental service in a specialized hospital, such as the Ohio Tuberculosis Hospital, is outlined. The description is based on the four main functions of the service, namely: administration, advisory, clinical and educational.

In the past decade, the health professions have become increasingly interested in the development of dentistry as a hospital service. Workshops, interprofessional committees, agencies of accreditation, and an increase in publications on hospital dentistry are indicative of this interest. What stimuli have moved dentistry to develop hospital dental services, internships, and residencies?

One answer to this question lies in dental education. The modern dental graduate is a product of a recognized college which has trained him to be cognizant of his responsibilities in the health program of his community. This education enables him to make sound decisions based on accepted principles of the healing arts. His responsibilities include the complete management of the oral cavity, for as it has been stated, "The limitations of dental practice are determined by the location of the disease and not by the nature of the problem or the method of treatment."[1]

Also, modern health services are planned to treat the whole patient. Present-day hospital services are expanding proportionally with the knowledge required for the treatment of disease. The interrelationship of one service to another is an accepted practice in hospital procedure—a practice designed to give the patient the best possible chance for complete recovery. Many hospitals include not only health services but also sociological services to complete the patient's readjustment. The modern hospital is the logical place for all of the services since they can be combined conveniently in the treatment of each patient.

Almost all other branches of health

services have been consulting with dentistry as a result of awareness of the relationship of good oral health and the welfare of the patient. "In all of these areas the dental profession has demonstrated the relationship of dental health to the total health of the individual. It has established dentistry as a basic health service in the health programs of the nation."[1] The question arises as to whether such a program can serve the hospitals' established services. Dentistry believes it can. A few of the more obvious advantages are: maintenance of dental health of chronically ill patients, relief of pain of dental origin for inpatients in general hospitals, early detection of systemic disease through oral diagnosis, treatment of oral foci of infection as an aid in management of total disease, and so forth. Conversely, the advantages gained by the dental profession are equally as important since hospital care of dental patients is a great asset to complete patient management.

The desirability of having dentistry as a hospital service is not a generally accepted conclusion. Doctors in both dentistry and medicine presently are engaged in formulating policies to facilitate the inclusion of dentistry into the complex organization of the hospital. The American Dental Association has established a Council on Hospital Dental Service to assist interested hospitals in the improvement of their dental services. This Council acts to maintain the high standards of the dental profession serving the hospitals' need. The strong feeling of the dental profession toward the entire project is expressed in the report of the Council on Hospital Dental Service, *Basic Standards of Hospital Dental Service:*

> The dental profession believes that the health care it renders is an essential part of the total health service. It has been recognized, also, that its services must be well integrated with those of the other health professions in order to provide the total health service for the individual patient. The modern hospital, marshalling as it does many professions, services, and facilities, provides a great challenge and opportunity for inter-professional cooperation in the service of the individual patient.[2]

The organization of the dental service depends on the extent of coverage required by the individual institution. In the larger hospitals and teaching hospitals, the division of the medical and dental staffs into more than minimal departments is desirable. Therefore, the dental department could be organized into sections conforming to recognized specialties. In the smaller hospitals, or hospitals where the principal activity centers around oral surgery, the service may be organized as a section of the surgery department coequal with the other surgical specialties.[2]

In 1953, a joint meeting was held between the Council on Hospital Dental Service and the Joint Commission on Accreditation of Hospitals. It was the opinion of the conferees that dental patients could be admitted to a surgical service by a member of the dental staff, provided this service is the responsibility of the chief of the surgery department. Furthermore, an adequate medical survey by a physician must be completed for each patient before dental surgery is performed.

The following statement was issued by the Joint Commission on Accreditation of Hospitals in its bulletin of December 1953:

> Depending upon the local situation and the qualifications of the individuals involved,

Contingent IID, Section 2, might be interpreted to mean that a "surgical service" may be the oral surgical service to which the members of the dental staff admit and discharge dental patients, provided that this service is the responsibility of the Chief of the Department of Surgery and that Section 3 of the *Standard* is complied with actively.[3]

The function of the dental service is controlled largely by the extent of services provided. However, these four main functions are essential:

Administration: to conduct the affairs of the dental service in accordance with the established administrative procedures of the hospital. *Advisory:* to act, through customary channels in an advisory capacity on all problems related to the dental health of the patient. *Clinical:* to render professional services to patients in accordance with the concepts of modern scientific dentistry and to evaluate these services periodically; to consult on dental matters with the other services. *Educational:* to provide, where feasible, an educational program for dental interns, dental residents, dental hygienists, dental assistants, and nurses; to provide training for junior staff members; to engage, when facilities permit, in teaching of graduate and postgraduate students who are preparing themselves for one of the specialties of dentistry.[3]

Obstacles to hospital dental services are being removed. However, one problem of prime importance remains to be solved: the cost of dental services. The cost of maintaining adequate dental services is high. Initial installation of equipment and operational expenditures often prove to be too much of a burden on the overtaxed hospital budget. In one instance this cost was covered in part by an active auxiliary which collected both money and equipment from interested people of the community.[4] Similar programs may be the solution for other hospitals; but these matters must be approached cautiously and soundly.

■ *Dental Service of the Ohio Tuberculosis Hospital*

Since the Ohio Tuberculosis Hospital is concerned primarily with the chronically ill inpatient, the nature of the dental service must undergo some modification. The basic functions remain the same. We must have an able administration, provide clinical services, give consultation service, and carry on an educational program. The service also must enter into the rehabilitation program for the patient's return home.

ADMINISTRATION—The Ohio Tuberculosis Hospital dental service varies from the general hospital in that the service is an independent function responsible directly to the hospital director. Since the primary cause for admission to this hospital is never for dental service, admissions or discharges are not made by the dental staff. The dental staff is small, consisting of a chief of dental service and a dental intern. Consultation privileges with the dental staff of University Hospital and the faculty of the College of Dentistry provide a complete coverage for each dental specialty.

ADVISORY—Advisory activity is carried on for those patients who wish to participate in the dental service. Because of the nature of the treatment for tuberculosis, the dental staff may only suggest treatment procedures. The medical staff then determines if these procedures conflict with the treatment planned for the patient. The final treatment plan is ap-

proved by the resident physician attending the patient. The medical staff asks for consultation with the dental staff in regard to pathologic conditions of the oral cavity.

CLINICAL SERVICE—An aseptic clinic technic is used to prevent the spread of disease to the staff or to other patients. The clinic is equipped with a modern dental unit and x-ray machine, and there is an annual budget allowance for purchase of new equipment or replacement of expendable items. Auxiliary personnel are provided by the nursing department of the hospital. The head nurse of the clinical division assumes the responsibility for these employees.

Weekly clinics include a diagnostic-admission clinic on Monday mornings, periodontic consultation clinic on Tuesday afternoons, and an oral surgery clinic on Friday mornings. Prosthodontic, orthodontic, oral pathology and pedodontic consultations are conducted when specifically indicated.

The primary service rendered is periodontal management, since few of our patients enjoy good oral hygiene. This is probably a reflection of the economic strata afflicted with tuberculosis, rather than an indirect extension of disease to the oral structures. The next most active services are oral surgery and prosthodontics. However, when favorable prognosis can be assured, every effort is made for oral rehabilitation. A denture service is provided if the patient is edentulous.

EDUCATION—Postgraduate basic science courses are required during the three school quarters academic year. One of the interesting and valuable applications of a hospital dental internship is the opportunity for postgraduate basic science study and research. Dental services develop in proportion to accomplishments in research. Staff personnel who use the hospitals as a center for professional activity should have a positive attitude toward postgraduate education and research.

The Ohio Tuberculosis Hospital postgraduate program is integrated with the postgraduate division, College of Dentistry, Ohio State University. The dental intern is enrolled as a professional postgraduate student. The academic courses emphasized are head and neck anatomy, oral pathology, and seminar in dentistry. The dental intern attends a formal lecture series conducted by the department of anatomy. A special problem in gross anatomy dissection of the head and neck is required for this course.

The dental intern is enrolled for postgraduate credit in head and neck anatomy in the division of oral surgery. This course is for two hours a week for three school quarters. It includes weekly three-dimensional slides, gross dissections and sagittal sections, and written examinations.

The intern attends postgraduate oral pathology courses for credit. This program presents advanced discussion of the clinical and histological characteristics of oral disease. Biopsy service specimens are reviewed. The postgraduate faculty also presents a weekly slide discussion and quiz session in oral and general pathology. These two sessions are augmented by private consultations with the oral pathologist of the College of Dentistry and chief of pathology for the Ohio Tuberculosis Hospital.

Dental seminar covers a broad area

of dentistry and is attended four hours a month for three school quarters. The seminar program is augmented with literature research at the University Health Center Library. Special fields of interest are investigated and papers are presented for review by the postgraduate faculty.

Undergraduate students at the College of Dentistry are given practical clinical experience in aseptic technics at the Dental Clinic of the Ohio Tuberculosis Hospital. Under the supervision of the staff, each dental student is taught the hospital routine and gains confidence in the use of surgical, clean and sterile technics. The same program is presented to the senior class of dental hygienists. The hygienists also are encouraged to enter into the patient rehabilitation program conducted by the hospital.

■ *Summary*

1. With the increase of interest in hospital dental services, the dental profession has established a logical and acceptable standard of dental services.

2. The problems involved in this growth and development are being handled through areas of interprofessional cooperation consistent with the newer concepts of total treatment-planning for the patient.

3. The dental service of the Ohio Tuberculosis Hospital is designed to meet these requirements within the limitations of the institution's facilities and needs.

4. Clinical and basic science classes are utilized to broaden the educational aspects of the internship.

Presented for credit in postgraduate dentistry, College of Dentistry, Ohio State University Health Center, Columbus, Ohio.

*Former dental intern, Ohio Tuberculosis Hospital, Ohio State University Health Center. Presently, staff dentist, Toledo Dental Dispensary.

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■ Age

Age should not have its face lifted but it should rather teach the world to admire its wrinkles as the etchings of experience and the firm lines of character.—*Ralph Barton Perry.*

Influence of alphaprodine hydrochloride on intravenous barbiturate induction dosage

■ *Richard J. DeLapa,* D.D.S., M.Sc., Tyndall AFB, Fla.*

Alphaprodine hydrochloride is a synthetic narcotic. An evaluation of its influence on intravenous barbiturate induction dosage was carried out. Sixty adult outpatients were used in this controlled study. The standard technic of induction with thiopental sodium was used; the loss of eyelid reflex was considered as the induction point. The use of alphaprodine hydrochloride reduced the dosage of induction thiopental sodium by nearly 40 per cent as compared to the control group. It was shown to produce apnea in 43 per cent of the patients and also reduced respiratory rate in 80 per cent of the patients. No other undesirable side effects were noted.

Alphaprodine hydrochloride is a synthetic narcotic. It has a rapid onset and a short duration of action with minimal side effects. As such, it merits investigation for use as a premedication agent for outpatients receiving general anesthesia for oral surgical procedures.

Alphaprodine has been described as resembling morphine sulfate in its action.[1-4] It acts rapidly to relieve pain, and the duration of effect is shorter than that of other narcotics.[5-8] There are minimal side effects, but synergistic depression of the respiration has resulted when it has been used with barbiturates.[9] The incidence of diaphoresis is observed more often and is more profuse than that found with meperidine.[8] The narcotic antagonists are effective antidotes for respiratory arrest due to alphaprodine.[10,11]

■ *Method*

Sixty adult outpatients constituted the population of this study. The patients were not specially selected but presented themselves for various oral surgery procedures to be performed under general anesthesia during the period of this investigation. Half of the patients served as controls and the remaining 30 patients constituted the test group. The mean age of the patients in the control group was 32 and in the test group it was 33. The mean weight of the patients in the control group was 147 pounds and in the test group it was 141 pounds. There were 15 females and 15 males in the control group, and 17 females and 13 males in the test group. No record was kept of the race of the patients.

The blood pressure, pulse and res-

pirations were recorded before premedication and induction and at the induction point. The control group received 0.4 mg. of atropine sulfate subcutaneously, and the test group received atropine sulfate 0.4 mg. and alphaprodine hydrochloride (Nisentil) subcutaneously. Alphaprodine hydrochloride 40 mg. was administered to patients with a body weight of 110 pounds with an increase or decrease of 5 mg. of alphaprodine per 10 pound body weight change, with a maximum dose of 60 mg. The premedication was given approximately 45 minutes prior to induction.

The standard technic of induction with thiopental sodium was used.[12] The loss of eyelid reflex was considered as the induction point.

■ *Results*

The mean systolic blood pressure in millimeters of mercury for the control group was 121 before premedication, 122 before induction and 112 at the induction point. The mean systolic blood pressure for the test group was 125 before premedication, 137 before induction and 123 at the induction point.

The mean diastolic blood pressure in millimeters of mercury for the control group was 77 before premedication, before induction and at the induction point. The mean diastolic blood pressure in millimeters of mercury for the test group was 81 before premedication, 87 before induction and 79 at the induction point.

The mean pulse rate per minute for the control group was 90 before premedication, 88 before induction and 103 at the induction point. The mean pulse rate per minute in the test group was 86 before predmedication and before induction and 93 at the induction point.

The mean respiratory rate per minute in the control group was 20 before premedication, 21 before induction and 21 at the induction point. The mean respiratory rate per minute in the test group was 19 before premedication, 16 before induction and 14 at the induction point. In the control group, one patient was apneic at the induction point, whereas in the test group 13 patients were apneic at the induction point. The maximum period of apnea was 90 seconds. The mean respiratory rate per minute at the induction point for the control group was based on 29 patients and for the test group it was based on 17 patients.

The mean number of cubic centimeters of induction thiopental sodium for the control group was 15.1 and for the test group it was 9.0. The minimal dose in cubic centimeters for the control group was 5 and for the test group it was 4. The maximum dose in cubic centimeters for the control group was 30 and for the test group it was 16.

No side effects such as nausea, vomiting or diaphoresis occurred in the test group.

■ *Discussion*

The mean systolic blood pressure varied only slightly in both groups. However, 7, or 23.3 per cent, of the patients in the test group had an increase in systolic blood pressure of from 20 to 40 mm. of mercury after premedication (Table 1). This was the opposite effect from what was expected. The cause was believed to be the decrease in the respiratory rate by the action of the narcotic,

Table 1 • Changes in blood pressure in millimeters of mercury after premedication, by number and per cent of patients

Group	−11 to −20		−1 to −10		0		+1 to +10		+11 to +20		+21 to +30		+31 to +40	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Systolic														
Control	2	6.6	9	30	8	26.6	4	13.3	5	16.6	2	6.6	—	—
Test	—	—	10	33.3	3	10	3	10	5	16.6	4	13.3	5	16.6
Diastolic														
Control	1	3.3	9	30	11	36.6	3	10	6	20	—	—	—	—
Test	2	6.6	6	20	6	20	5	16.6	9	30	2	6.6	—	—

which resulted in a moderate increase of carbon dioxide retention in the blood and which affected the vasomotor center, causing a general, moderate vascoconstriction.

At the induction point 20, or 66.6 per cent, of the patients in the control group and 24, or 80 per cent, of the patients in the test group had a decrease in systolic blood pressure (Table 2). This decrease was supposedly caused by the depressant action of the barbiturate on the cardiovascular system.[13]

There were no significant variations in the mean diastolic blood pressure in either the control or test group. No patient had an increase of diastolic blood pressure in millimeters of mercury of more than 30 or a decrease of more than 20 after premedication, or an increase of more than 20 or a decrease of more than 30 at the induction point (Tables 1 and 2).

Atropine sulfate is a parasympathetic blocking agent and should increase pulse rate by inhibition of the vagus nerve. Subcutaneous atropine sulfate 0.4 mg. did not increase the mean pulse rate in the control group before induction. When atropine sulfate and alphaprodine hydrochloride were used subcutaneously, no increase in pulse rate was found in the test group before induction. However, the mean pulse rate in the control group at

Table 2 • Changes in blood pressure in millimeters of mercury at induction point based on blood pressure after premedication, by number and per cent of patients

Group	−31 to −40		−21 to −30		−11 to −20		−1 to −10		0		+1 to +10		+11 to +20		+21 to +30	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Systolic																
Control	—	—	1	3.3	13	43.3	6	20	4	13.3	2	6.6	4	13.3	—	—
Test	6	20	5	16.6	9	30	4	13.3	3	10	2	6.6	—	—	1	3.3
Diastolic																
Control	—	—	—	—	—	—	7	23.3	16	53.3	1	3.3	6	20	—	—
Test	—	—	1	3.3	10	33.3	9	30	7	23.3	2	6.6	1	3.3	—	—

Table 3 • Changes in pulse rate per minute after premedication, by number and per cent of patients

Group	−21 to −30		−11 to −20		−1 to −10		0		+1 to +10		+11 to +20		+21 to +30		+31 to +40	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control	2	6.6	8	26.6	6	20	9	30	—	—	3	10	2	6.6	—	—
Test	2	6.6	9	30	2	6.6	5	16.6	5	16.6	3	10	2	6.6	2	6.6

Table 4 • Changes in pulse rate per minute at induction point, based on pulse rate after premedication, by number and per cent of patients

Group	−21 to −30		−11 to −20		−1 to −10		0		+1 to +10		+11 to +20		+21 to +30		+31 to +40		+41 to +50	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control	—	—	1	3.3	2	6.6	5	16.6	3	10	8	26.6	6	20	3	10	2	6.6
Test	1	3.3	4	13.3	5	16.6	4	13.3	7	23.3	4	13.3	4	13.3	—	—	1	3.3

Table 5 • Changes in respiratory rate per minute after premedication, by number and per cent of patients

Group	−11 to −15		−6 to −10		−1 to −5		0		+1 to +5		+6 to +10		+11 to +15	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control	—	—	—	—	5	16.6	14	46.6	7	23.3	3	10	1	3.3
Test	2	6.6	4	13.3	17	56.6	6	20	1	3.3	—	—	—	—

induction point increased 15 beats per minute, and in the test group it increased 7 beats per minute (Tables 3 and 4). This increase was associated with decrease in respiratory minute volume in 33 patients, and apnea in 10 of these patients at induction point. It is probable that decreased circulating blood volume due to depression and muscular relaxation from thiopental sodium resulted in decreased arterial blood oxygen saturation and decreased cardiac output. However, none of these were measured in this study.

The mean respiratory rate per minute in the control group remained essentially unchanged. However, in the test group the mean respiratory rate per minute decreased from 19 before premedication to 16 before induction and to 14 at the induction point. This decrease was interpreted to be due to the direct effect of the narcotic on the respiratory center. Also, 13 patients in the test group were apneic at the induction point whereas only one patient in the control group was so affected (Tables 5 and 6). This result

Table 6 • Changes in respiratory rate per minute at induction point, based on respiratory rate per minute after premedication, by number and per cent of patients

Group	Apnea		−11 to −15		−6 to −10		−1 to −5		0		+1 to +5		+6 to +10		+11 to +15	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control	1	3.3	1	3.3	2	6.6	5	16.6	12	40	6	20	3	10	—	—
Test	13	43.3	—	—	7	23.3	4	13.3	3	10	2	6.6	—	—	1	3.3

Table 7 • Cubic centimeters of induction thiopental sodium, by number and per cent of patients

Group	1 to 5 cc.		6 to 10 cc.		11 to 15 cc.		16 to 20 cc.		21 to 25 cc.		26 to 30 cc.	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control	1	3.3	4	13.3	13	43.3	7	23.3	3	10	2	6.6
Test	2	6.6	21	70	6	20	1	3.3	—	—	—	—

substantiated previous work which showed that alphaprodine used in conjunction with a barbiturate produced synergistic depression of respiration. It is concluded from this result that when alphaprodine and a barbiturate are used together for premedication, careful observation of the patient's respiratory tidal volume and respiratory rate is mandatory.

The number of cubic centimeters of induction thiopental sodium was 39.9 per cent lower in the test group than in the control group (Table 7). This difference was interpreted to be due to depression of cerebral cortex and medulla by alphaprodine, reducing the amount of barbiturate required.

■ *Conclusions*

1. The use of alphaprodine hydrochloride reduced the dosage of induction thiopental sodium by 39.9 per cent as compared to the control group.

2. Alphaprodine hydrochloride used as premedication with thiopental sodium induction produced apnea in 43.3 per cent of the patients and reduced the respiratory rate in 80 per cent of the patients.

3. Alphaprodine produced no side effects of nausea, vomiting or diaphoresis in 30 patients.

4. No significant changes in blood pressure or pulse rate resulted from the use of alphaprodine.

The opinions or assertions contained herein are those of the author and are not to be construed as official or as reflecting the view of the Department of the Air Force or the Air Service at large.

Thesis submitted in partial fulfillment of the requirements for a degree of Master of Science (Oral Surgery) at Ohio State University.

The Nisentil used in this study was furnished through the courtesy of Hoffmann-La Roche, Inc.

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■ Race for Survival

Man in his arrogance may boast that the battle is to the strong, that pity and affection are signs of weakness. . . . Man, in the achievement of a unique gift—a thinking brain capable of weighing stars or atoms—cannot grow that brain in the nine months before birth. It is, however, a peculiarly plastic brain, intended to receive impressions from the social world around it. Instinct, unlike the case in the world of animals, is here reduced to a minimum. This brain must grow and learn, be able to profit by experience . . .

Is the price of acquiring brains, brains to look before and after in the universe, only to mean subservience to man after escaping subservience to nature . . . ? Is it to mean acquiescence in the plans of those clever intellects who talk glibly of psychological "break-throughs" and the subliminal control of nations? Is it for this that men have labored up the dark pathway behind us and died often and blindly for some vision they could scarcely see? A society has an image of itself, its way of life. This image is a wavering, composite picture reflected from millions of minds. If the image is largely compounded of the events of the present; if tradition is weak, the past forgotten, that image can alter by subtle degrees. . . . The humane tradition—arts, letters, philosophy, the social sciences—threatens to be ignored as unrealistic in what has become a technological race for survival . . .

Man, unlike the animal, is aware of the nature of his society. His conscious image of it is tremendously important in shaping what it will become. . . . Man, whether he engages in war or not, is in a pyramiding technological society whose values are largely directed outward upon things. The important fact in such a material age is that we do not abandon or forget that man has always sought to transcend himself spiritually, and that this is part of his strange heritage. It is a heritage which must be preserved in our schools and churches, for in a society without deep historical memory, the future ceases to exist and the present becomes a meaningless cacophony. A future worth contemplating will not be achieved solely by flights to the far side of the moon. It will not be found in space. It will be achieved, if it is achieved at all, only in our individual hearts. This is the choice that has been presented man, as a free agent, as one who can look before and after.—*L. Eiseley, An Evolutionist Looks at Modern Man. The Saturday Evening Post, April 26, 1959.*

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CASE REPORTS

Sarcoidosis lesions primary in the oral cavity: *report of a case*

■ *Steve Kolas,* D.D.S., M.Sc., and William C. Roche,† D.D.S., Columbus, Ohio*

Skin lesions of sarcoidosis were first described by Hutchinson in 1795. Microscopic descriptions by Boeck in 1899 employed the use of the term, sarcoid (fleshlike). Schaumann[1] (1914) was first to point out the systemic character of sarcoidosis. It has been variously called lymphogranulomatosis, uveoparotid fever and Heerfordt's disease.[2,3] These terms serve to show the variable clinical features and course of this disease. This disturbance is ordinarily a chronic benign systemic granulomatous disease (involving chiefly lymphoid and lung tissue).[4] On rare occasions the oral structures may be the only region affected. There is a paucity of reports of oral findings in the literature.[5] This report is concerned with a case of sarcoidosis in which lesions were evident only in the oral cavity.

HISTORY—A 15 year old white boy was admitted on medical service at University Hospital, Ohio State University. He had a history of diabetes mellitus of nine years' duration. He had had several teeth removed within the past six months. Three weeks prior to admission the patient had noticed a "lump" near the fundus of the socket of the right maxillary central incisor. A few days later he noticed "lumps" developing above the apex of the left maxillary central incisor, in the left mandibular buccal shelf region, and in the right cheek below the level of the parotid duct against the anterior margin of the masseter muscle.

PHYSICAL EXAMINATION—The patient was an apparently healthy, well developed boy. The oral nodular masses were visible and palpable. The overlying mucosa was of normal color and nontender.

LABORATORY DATA—The laboratory data was as follows: "Hemoglobin 14.6 Gm. per each 100 cc., hematocrit 46 per cent, white blood cells 7,750 with neutrophils 44 per cent, lymphocytes 50 per cent, eosinophils 5 per cent, monocytes 1 per cent. Sedimentation rate was 10 mm. per hour. Fasting blood sugar 165 mg. on one occasion and 263 mg. per each 100 cc. on another. Blood-urea-nitrogen 14 mg. per each 100 cc., inorganic phosphorus, 5.9 per cent mg., alkaline phosphatase 18.2, total cholesterol 178, cholesterols esters 76 per cent, total protein 6.1 cm. per each 100 cc., with albumin 4.1, globulin 2, calcium 10 mg. per each 100 cc. Urinalysis reported a specific gravity of 1.030, pH 5, sugar 3 plus with occasional white blood cells per high powered field. The stools were negative for occult blood."

ROENTGENOGRAPHIC EXAMINATION—Complete oral roentgenograms revealed multiple carious lesions involving most of the remain-

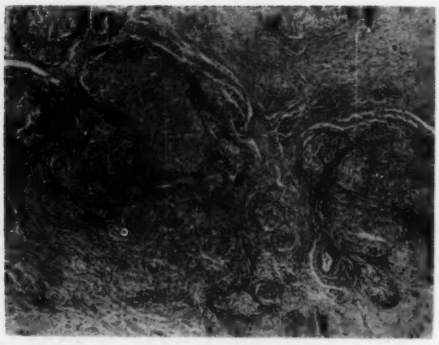

Fig. 1—View showing multiple, discrete, well circumscribed areas of granulomatous reaction

ing teeth and slight periodontal alveolar bone loss. There was no evidence of bone rarefaction in association with the nodular masses. Chest and skull films showed no pathosis.

HOSPITAL COURSE AND TREATMENT—Upon admission, the patient was fed a diabetic diet. The urine was checked for sugar and acetone before meals and at bedtime. Insulin was given every morning before breakfast.

OPERATION—During general anesthesia, a tissue specimen was removed intraorally from each of the four nodules for biopsy.

POSTOPERATIVE COURSE—The oral operative sites had moderate edema. Healing was uncomplicated. For seven days postoperatively the fasting blood sugar followed a hectic course, varying between 300 and 339 mg. per each 100 cc. Insulin dosage was readjusted. The patient was discharged from the hospital on the twelfth hospital day with stable vital signs.

HISTOPATHOLOGIC REPORT—Report of the examination of intraoral nodular masses was as follows:

"1. Excised tissue from right cheek: fatty areolar tissue with focal noncaseating granulomas (Boeck's sarcoid).

"2. Excised tissue designated labial vestibule: noncaseating granulomatous inflammation in reactive fibrous tissue and muscle (Boeck's sarcoid).

"3. Excised tissue designated labial vestibule: noncaseating granulomatous inflammation infiltrating voluntary muscle (Boeck's sarcoid).

"4. Excised tissue designated left buccal vestibule: noncaseating granulomatous inflammation in voluntary muscle and fat (Boeck's sarcoid).

"The diagnosis is Boeck's sarcoid.

"Comment—The histologic structure of these multiple biopsies is characteristic of the nodular granulomas which do not show evident caseation and which are designated Boeck's sarcoid. One of the biopsy specimens does show an area of central necrosis but this has more the appearance of an ischemic phenomenon than of an intrinsic necrotizing tendency within the granulomatous lesion."

The patient was readmitted to University Hospital and complete surgical excision of the nodular masses was done. These masses were fairly well circumscribed and rather easily separated from the surrounding normal tissue. All but four of the remaining teeth were removed and the oral tissues were prepared for prosthetic appliances. The patient was given antibiotic therapy. Postoperative healing was uneventful.

DISCUSSION—Sarcoidosis is ordinarily a chronic granulomatous systemic disease (Fig. 1) characterized by tubercle-like lesions comprised of epithelioid and giant type cells.[1,4] Usually no caseation is evident. Protean clinical manifestations are seen; some persons are affected severely and others slightly. Usually the disease follows a benign, prolonged irregular course with frequent spontaneous remissions. A rapid downhill course leading to death is uncommon. When death does occur it is usually the result of associated intercurrent infection or chronic cor pulmonale caused by diffuse lung fibrosis. The variable clinical picture of this disease is influenced by the severity of the granulomatous reaction, the extent of involvement of the part or parts affected and secondary complications.

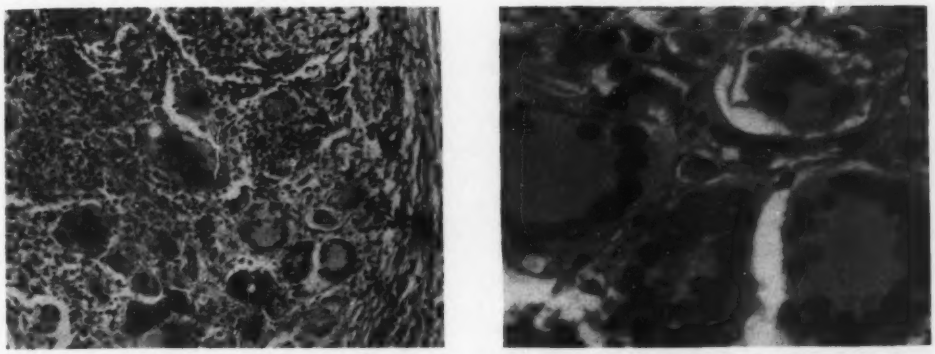

Fig. 2—Left: Photomicrograph showing singular "tubercle" with characteristic epithelioid and giant cell type cells and some lymphocytes. Note lack of caseation. Fibrillar components appear intact. Right: Epithelioid and giant cells of both foreign body and Langhans' type

This uncommon disease is seen in practically any age group but most frequently in the third and fourth decades. It occurs twice as frequently in men as in women and more often in Negroes than in whites.

Although any organ may be affected, lymphoid tissue seems particularly prone to involvement. Lung tissue, skin, mucosa, bones, eyes, liver, spleen and parotid glands frequently are involved.

Skin and mucous membrane lesions are encountered in approximately one half of the patients. The clinical appearance of cutaneous lesions varies. Some are discrete subcutaneous nodules, others are slightly elevated erythematous to violaceous plaques. Some may be red flat scaly lesions.[2,4] Oral lesions are reported in a scant number of cases.[5] The lesions described involving the oral mucosa are reported as vesicular or bleblike in nature, containing a clear yellow fluid.[2,3]

Involvement of the parotid glands may result in facial swelling and asymmetry. Salivary flow may be diminished. As the uveal tracts of the eye become inflamed, visual impairment ensues. The combined parotid gland and eye involvement constitutes uveoparotitis.[1] Roentgenograms, particularly of the phalanges of the hands and feet, may show discrete or diffuse rarefactions. The discrete entities are ovoid and punched-out areas. The diffuse rarefactions may present a reticular pattern. Sometimes the mandible may be perceptibly involved.

Blood studies may show a considerable elevation of gamma globulin. With hyperglobulinemia slight to moderate elevations of monocytes, eosinophils, sedimentation rate, serum calcium and alkaline phosphatase may occur. Slight microcytic anemia and leukopenia may be observed.

Summation of the clinical findings that are more consistently seen in sarcoidosis include: (1) discrete and disseminated skin lesions; (2) hyperglobulinemia, (3) uveoparotitis and (4) bone involvement, particularly of the bones of the hands and feet, roentgenographically seen as variable rarefactions. In the patient concerned in this report, only oral submucosal discrete nodular masses were found.

The characteristic microscopic lesion of sarcoidosis is described as a noncaseating "tubercle." The usual granulomatous tubercle is a discrete, well circumscribed reaction frequently outlined by a fibrous margin (Fig. 2, left). Cell types characteristically observed are epithelioid cells and giant cells of the foreign body and Langhans' type (Fig. 2, right). Occasional lymphocytes and neutrophils may be evident. Reticulin fibers remain intact and do not undergo the degeneration and fragmentation seen in caseous necrosis. Ordinarily the tissues between the various aggregates of

granulomatous reaction appear uninvolved. The giant cells seen in the tubercle may contain inclusion bodies described as (1) asteroid or (2) laminated ovoid Schaumann's bodies. However, these are nonspecific inclusions and are not pathognomonic of sarcoidosis.[4]

The etiology of sarcoidosis is unknown. The claim that it is an "atypical variant" of tuberculosis is not proved. Unequivocal demonstration and isolation of the characteristic acid-fast tubercle bacillus and the successful animal inoculation with it is yet to be shown.[4]

Although caseation is not a usual observation in sarcoidosis, some observers claim that caseation may occur occasionally. Therefore, when in noncaseating sarcoidosis occasional central necrosis is evident, possible concomitant tuberculosis must be ruled out. It is well established that the tuberculin skin test is not positive in persons currently having sarcoidosis and tuberculosis.[4] Such a negative result is evaluated by some as a hint of anergy. The suggestion has been made that sarcoidosis may be a variant of other granulomatous diseases such as leprosy, syphilis, brucellosis or some form of mycosis. Again, no proof is available. Some investigators point to the elevated plasma gamma globulin level as an indication of hypersensitivity toward an unknown allergen.[1,4] Here, too, no proof is available. The etiology is still unknown.

SUMMARY—A patient was seen with multiple nodular oral mucosal masses (Boeck's sarcoid). These masses presented no obvious clinical diagnostic characteristics.

Periodic follow-up should be maintained in such cases to determine if extraoral extension of the disease occurs. Consultation and cooperation with the medical service should be utilized.

The opinions or assertions contained in this article are those of the author and are not to be construed as official or as reflecting the view of the Department of the Air Force or the air service at large.

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■ Quackery in Nutrition

The most widespread quackery in the United States today is in the field of nutrition. The American Medical Association says it is costing some ten million Americans 500 million dollars each year. This racket is based on misstatement of the facts of the science of nutrition. More people seem to believe more bunk about food and nutrition than about any other single topic in the health field—and perhaps any other field. . . . Food faddism today has aspects of an organized movement that is self-supporting and actively seeking new converts. . . . An especially disturbing feature of food faddism is persistent emphasis on the theme that the American food supply, unmatched in quality throughout the world, is deficient, over-processed, or poisoned by fertilizers, pesticides, and food additives. There are indeed serious new problems of food protection brought about by changing technology that are under constant study, but nothing to warrant the grossly irresponsible and inaccurate statements which have appeared in some faddist books and sensational magazines.—*Wallace F. Janssen, Quackery and the News. Pub. Health Rep. 74:635 July 1959.*

Dentigerous cyst with ameloblastomatous change.
report of case

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This case report emphasizes the importance of histological examination of all surgical specimens. The preoperative diagnosis in this instance was dentigerous cyst of the mandibular third molar region on the right side. The surgical specimen on microscopic examination proved to be a dentigerous cyst which contained ameloblastomatous tissue.

REPORT OF CASE—The patient, a 16 year old girl, was first seen in the orthodontic clinic, College of Dentistry, Ohio State University. Routine full mouth roentgenograms revealed a radiolucency enclosing an unerupted mandibular right third molar (Fig. 1). There was no other evidence of a pathologic condition in the mandible or maxilla. The patient was admitted to the oral surgery service, University Hospital, Ohio State University Health Center. Physical examination and laboratory findings were within normal limits.

While the patient was under general anesthesia, the cyst was enucleated and both mandibular right and left third molars were removed. The soft tissue surgical specimen resembled a dentigerous cyst. However, on microscopic examination the specimen was found to contain ameloblastomatous tissue (Fig. 2). The postoperative hospital course was uneventful, and the patient was discharged 36

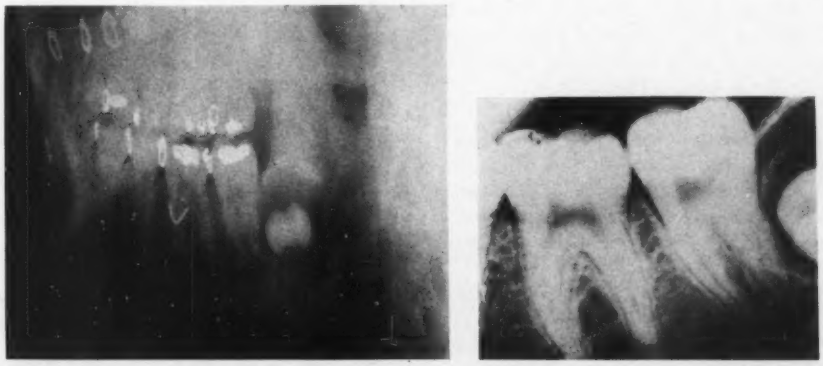

Fig. 1—Preoperative views

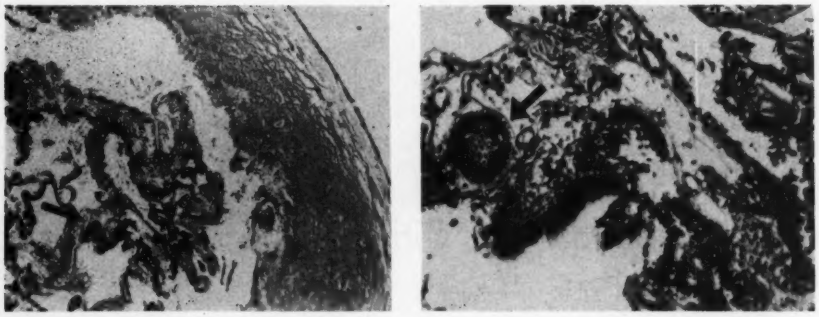

Fig. 2—Biopsy specimen. Left: Ameloblastomatous tissue. Right: Enlargement of view at left

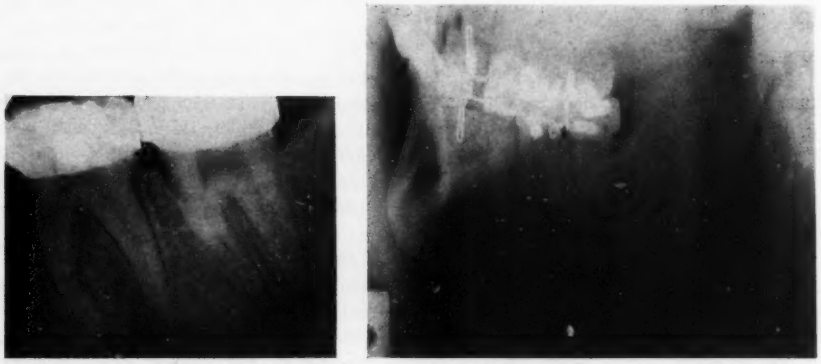

Fig. 3—Views 12 months postoperatively

hours after the surgical procedure. Roentgenograms taken 4 and 12 months postoperatively revealed normal bone architecture without recurrence of the tumor (Fig. 3).

MICROSCOPIC DESCRIPTION—The surgical specimen consisted of a cystic mass which contained epithelial cells arranged in solid nests and cords within the fibrous wall. Ameloblastic type cells and stellate reticulum also were seen.

DISCUSSION—Cahn,[1] in 1933, reported a case of ameloblastoma originating in the wall of a dentigerous cyst, and other cases have subsequently been recognized as developing in this fashion.[2] This case is being reported to re-emphasize the dangerous potential of dentigerous cysts and the need for microscopic examination of all surgical specimens.—845 *Eighth Street N.E.*

The opinions or assertions contained herein are those of the author and are not to be construed as official or as reflecting the view of the Department of the Air Force or the Air Service at large.

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Ameloblastofibroma of the mandible:
report of a case

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Tumors of odontogenic origin are perplexingly diverse in nature, and are of particular interest to the oral surgeon. These neoplasms may arise from ectodermal or from mesodermal odontogenic tissues or concomitantly from both.[1]

The ameloblastoma is deservedly the most notorious of the group and has its own variable character. When both ameloblastic and fibrogenic neoplastic proliferation occurs in a single lesion a mixed odontogenic tumor results. An example of the latter type is an ameloblastofibroma.

HISTORY—An 11 year old girl had had a noticeable swelling of the left side of her face and cheek for approximately one year. During roentgenographic examination, her dentist discovered a large area of radiolucency in the left mandibular molar region, whereupon he proceeded to remove several carious teeth from the involved region. He then referred the patient to the division of oral surgery, College of Dentistry, Ohio State University. She was admitted to the oral surgery service at the University Hospital on October 25, 1955.

PHYSICAL EXAMINATION—The patient was a thin, malnourished, white girl with a large swelling of the left side of her face. The enlargement was nontender and there was no associated lymphadenopathy. Intraoral examination disclosed recent extraction wounds in the left mandibular molar region and expansion of the body of the mandible.

Results of laboratory studies were within normal limits.

ROENTGENOGRAPHIC EXAMINATION—Roentgenographic examination disclosed a large, unilocular, cystic type radiolucent lesion of the left side of the mandible involving the body and ascending ramus with expansion of the cortical plate (Fig. 1). Two molar teeth crowns were observed lying near the inferior border of the mandible and seemingly were contained within the radiolucent region. Tentative clinical impressions were (1) dentigerous cyst or (2) ameloblastoma.

OPERATION—Under general anesthesia, an incision was made along the crest of the mandibular ridge which extended from the coronoid process downward and forward around the necks of the anterior teeth. A mucoperiosteal flap was reflected buccally exposing the thinned-out mandibular bone. A window approximately 3 cm. by 2 cm. was cut in the superior aspect of the mandible and a solid fibrous, gritty mass was visualized. A large triangular piece of this mass was removed and sent to the pathology laboratory for frozen section examination. The tentative diagnosis was "odontogenic fibroma with no malignant tendencies." The tumor mass, therefore, was

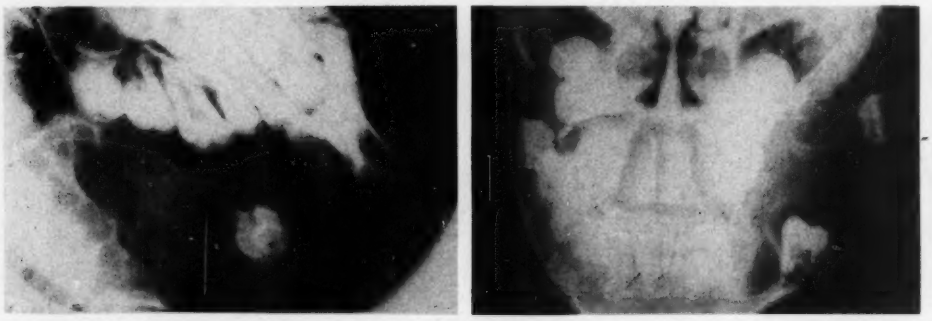

Fig. 1—Left: Preoperative left lateral view of jaw demonstrating expanding radiolucent lesion and displaced teeth. Right: Preoperative posteroanterior view of ameloblastoma of mandible

enucleated from the surrounding bone. It was removed cleanly and left a smooth surface of the mandible surrounding the cavity. There was no evidence that the tumor had invaded the soft tissue or surrounding bony tissue. The two embedded teeth which had been pushed aside by the tumor mass were removed from the cavity and the edges of the bone and soft tissue were trimmed and smoothed. The cavity was partially packed with Gelfoam and saturated with 1,000,000 units of penicillin. The superior aspect of the cavity was packed with iodoform gauze and one end was left extending through the mucosa. The mucoperiosteal flap was repositioned and sutured tightly with no. 000 silk. In order to stabilize the mandible and reduce the possibility of a fractured jaw, Ivy loops were placed in each quadrant of the mouth. The jaw was then immobilized by means of intermaxillary elastic traction. Blood loss was 400 cc. and the patient received 500 cc. of whole blood during the procedure.

Fig. 2—Intraoral view taken 1½ years after operation showing healed alveolar ridge

HISTOPATHOLOGICAL STUDY—Examination of hematoxylin and eosin stained tissue sections and consultation with the oral pathology staff indicated that more odontogenic epithelium was present than had been thought after viewing the frozen sections. The report of tissue analysis was as follows:

"This specimen is a large mass of soft tissue comprised chiefly of a young type connective tissue. It is moderately collagenic and shows an abundance of stellate type cells. This primitive appearing mass is slightly vascular. It is transversed in some areas by long, slender cords of epithelium whereas other portions exhibit nests or islands of epithelial cells. Furthermore, epithelial structures are seen that appear as enamel organs lined by ameloblastic type cells and reflect a central area comparable to a stellate reticulum. This is a graphic picture showing a mixed neoplastic proliferation of odontogenic epithelial and connective tissues. Diagnosis is ameloblastofibroma."

The patient was returned to the operating room for further biopsy of surrounding bone and removal of teeth adjacent to the

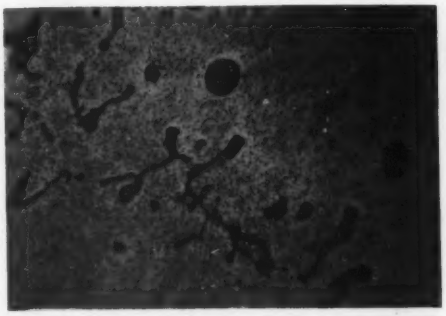

Fig. 3—Photomicrograph showing odontogenic epithelium and connective tissue components of tumor

tumor region. The report of microscopic analysis of the specimen taken at this procedure indicated that no additional tumor tissue was evident.

POSTOPERATIVE COURSE—The wound was irrigated and dressings changed at 48 hour intervals. The patient was discharged from the hospital 11 days after the second operative procedure. Approximately one half of the bony cavity was filled with healthy granulation tissue at this time. The intermaxillary wiring and Ivy loops were removed prior to her discharge. The patient was followed in the out-patient department and tumor clinic and seen at increasingly longer intervals. The cavity gradually filled completely and the bony ridge returned to a normal shape (Fig. 2). Roentgenograms taken February 18, 1957, showed complete bony regeneration (Fig. 3,4). The face of the patient was bilaterally symmetrical. The patient continues to be followed at semiannual intervals. The clinical and roentgenographic examinations show no evidence of recurrence of the disease.

DISCUSSION—The ameloblastofibroma is considered a mixed soft odontogenic tumor.[1-3] Both germ layers (epithelial and mesenchymal) of the odontogenic apparatus participate in the neoplastic growth.[1] It is a benign, slow growing lesion which enlarges by expansion and is not particularly prone to local infiltration. Being a central lesion (that is, in bone), its expansive growth causes bone rarefaction. Roentgenographically, the rarefaction is usually seen as a unilocular cystic radiolucency with a regular margin. However, multilocular patterns comparable to those of the simple (that is, solid or cystic type) ameloblastoma may be seen. Grossly, the ameloblastofibroma usually is firm, rather well circumscribed and tends to separate readily from bone. Microscopically, both the epithelium and connective tissue are seen to be engaged in neoplastic growth. The connective tissue element, appearing much like the primitive dental papillae, is the predominant tissue. It is quite cellular with stellate type fibroblasts. The collagen content is variable and vascularity is slight. The epithelial component is somewhat less than that usually seen in the simple ameloblastoma. Nevertheless, it is widely dispersed in varying amounts throughout the tumor. The epithelium may be seen in strands or cords reminiscent of the dental lamina. Enamel organ-like structures with ameloblastic type cells may be seen too. Active epithelial infiltration of the adjacent bone is not characteristic.

It has been suggested that the ameloblastofibroma be classed as a distinct and separate entity from the simple ameloblastoma.[3] The following factors support this contention:

1. Although ameloblastomatous in nature, the ameloblastofibroma is considered a mixed odontogenic tumor.[1]

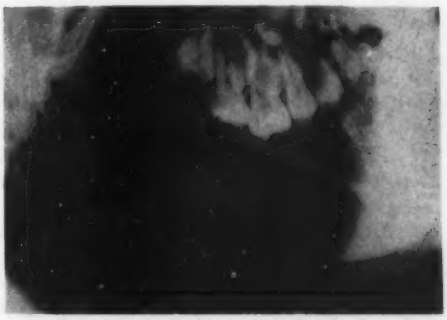

Fig. 4—Left lateral view taken February 18, 1957 (1½ years postoperatively) showing regeneration of bone and return of mandible to normal contour

2. It occurs in somewhat younger patients, the average age being approximately 17 years, whereas for the simple ameloblastoma the average age of patients is about 38.[2,3]

3. It reputedly grows more slowly and is not prone to local trabecular infiltration as is the simple ameloblastoma.[4]

4. It is not as persistent nor as likely to recur after conservative removal (enucleation).[3]

The ameloblastofibroma deservedly should be treated as a distinct and separate entity. The mere use of the term "ameloblastoma" does not extend authority to the surgeon to perform radical resection. Although it is generally true that the simple ameloblastoma is rather frequently aggressively treated, each problem should be handled according to the dictates of the case.

The prognosis for an ameloblastofibroma is stated to be excellent.[3] To have radically treated the child cited in this report by hemimandibulectomy would have been a tragedy.

SUMMARY—An ameloblastofibroma was removed from the left side of the mandible of an 11 year old girl. No recurrence of the tumor has been evident after surgery. The clinical aspect, gross and histologic features and classification of the tumor are discussed as well as the prognosis and suggested treatment.

*Formerly resident in oral surgery, University Hospital, Ohio State University Health Center. At present, assistant professor in oral surgery, College of Dentistry, Ohio State University. Member of active staff in oral surgery, University Hospital.

†Formerly fellow in oral surgery, University Hospital, Ohio State University Health Center. At present, associate professor and chairman, oral pathology department, College of Dentistry, Ohio State University.

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■ Speakers and Audience

Most listeners to papers read at professional meetings remember only from one-sixth to one-fourth of what the essayist wants to communicate. This was established by a serial investigation of verbal communication, made at the University of Minnesota.

Most essayists speak too slowly, giving their hearers' minds a chance to wander. By the time the essayist finished speaking, the average listener will remember only half of what he had said. Of the remaining half, the listener will forget from one-third to one-half within the next eight hours.

This is because most professional men can absorb scientific information much faster than the average speaker, with his 125 words per minute speech, is able to say. The listener's attention is, therefore, permitted to wander away from the subject as well as from the speaker.

Because it is difficult to change the speaker's habits and delivery, listeners should practice the following rules to retain more of what they hear: (1) they should watch the speaker's facial expressions and gestures; (2) they should listen closely for changes in his tone of voice; (3) they should attempt to insert the hidden meanings behind his words; (4) they should go back over the points the speaker already has made; (5) they should try to anticipate the conclusions he will make, and (6) they should try to determine whether his arguments and conclusions are based on solid facts and are logically constructed.—*Ralph G. Nichols. Science Digest 45:21 May 1959.*

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EDITORIALS

Research as part of graduate training

THE ROLE OF RESEARCH in oral surgery is vitally important; not only is it important in the discovery and development of drugs and technics which immediately benefit man—basic as that role is—but it is equally important in the graduate education of the oral surgery trainee.

Only through the appreciation of the principles of research can a proper discipline of mind be developed by the aspirant. The stern reality of facts and statistics when combined with the dreams of surgical conquest produce in the trainee an effect of prime importance not only to the development of his operative skill but to the development of mature judgment in evaluating the oral surgical literature.

It has been said that no active, well-trained practitioner of the healing arts ever ceases to indulge in some form of clinical research. This is as it should be, for clinical experience is the stimulant that brings out the need for scientific advancement. When the time arrives in which oral surgeons will receive, as part of their graduate training, a basic, even though a brief, grounding in research, another great step will have been taken in the development of a properly educated practitioner of oral surgery. Such an individual, throughout his professional life, will not only continue to engage in well conceived clinical research but he will be a more stable and better informed representative of the profession—one who will be infinitely more able to contribute to the health of those who are dependent on his care.—*Fred A. Henny.*

■ THE MANAGEMENT OF ORAL DISEASE. By Joseph L. Bernier, D.D.S., M.S., F.D.S., R.C.S. (Eng.) Second edition. 875 pages with 1031 illustrations. Index. $15. St. Louis, Mo., The C. V. Mosby Co., 1959.

Just four short years has produced the second edition of Colonel Bernier's excellent textbook on oral diseases. This certainly attests to the need for, and welcome reception given to, the first edition by the dental and medical professions.

The layout of the second edition is exactly the same as the first, carrying the reader through 22 comprehensive chapters covering about all of the known diseases of the mouth and jaws. The text material remains essentially unchanged. The subjects are discussed from the etiological, clinical, and histopathological standpoint.

The new outstanding features of the second edition include: the two years' investigation at the Armed Forces Institute of Pathology into the pulpal changes related to high speed instrumentation; the etiology of lymphoid lesions of the salivary glands; the latest information on the pathology of caries and periodontal diseases, and finally the latest concepts in the treatment and management of oral diseases.

This edition, like the first, is abundantly supplied with many old and some new illustrations. Particularly impressive are the reproductions of the roentgenograms and microphotographs. Each chapter has an extensive bibliography affording almost unlimited reference material to any oral condition.

This edition is highly recommended to all professional persons and students undertaking care and study of oral diseases. However, except for institutional libraries, it is questionable whether the advances made from 1955 are sufficient for an individual to need to possess both editions.—*Richard C. Baumbach.*

■ A MANUAL OF ANAESTHETIC TECHNIQUES By William J. Pryor. Second edition. 228 pages with 75 illustrations. Index and references. $7. Baltimore, The Williams & Wilkins Co., 1959.

This edition is a rather complete revision of the first. The chapter on ether has been brought up to date and one on local analgesia added.

It is a useful text for those students who are starting their training, and for a quick reference source of practical technics. It does not discuss theory or physiology of anesthesia.

There is an outstanding chapter on equipment which shows in picture form, with text, all of the everyday armamentarium of the anesthetist. Another chapter which deserves special mention is the one entitled "Mechanical and Physiological Aspects of Anaesthesia." In this chapter the reader will find a very practical description and explanation of the physics of anesthesia and anesthetic equipment.

Of special interest to oral surgeons and general practitioners of dentistry is a chapter on dental anesthesia. This is a thorough and informative description.

On page 89, under the description of controlled respiration, there is a picture showing the anesthetist several feet away from the patient with the rebreathing bag resting in his lap. This technic leaves much to be desired inasmuch as the anesthetist is not within reach of the patient's pulse. Most anesthesiologists will agree that a pulse should be felt or heard (by stethoscope or cardiac monitor) at all times, because the heart can cease before respirations. With the anesthetist in the position shown in figure 49, the patient could expire while the anesthetist continues to "control his respirations." Obviously this is shown to stress a particular technic and is not the usual procedure.

This is an outstanding reference and contribution to the literature and would be a useful addition to the dentist's or physician's library.—*James B. Edwards.*

Announcements

■ Exhibits Invited at 42nd Annual Meeting of Oral Surgeons

For the first time at an annual meeting, the American Society of Oral Surgeons has invited exhibits. It has been announced that adequate exhibit space has been assigned at the Westward Ho Hotel, Phoenix, Ariz., for the forty-second annual meeting which will be held October 12-15.

A complete exhibits prospectus will be mailed on request to any organization supplying equipment, materials or services used by the oral surgeon and meeting official standards of the American Dental Association.

At the forty-first annual meeting held in New York, membership in the society was announced as 947. Officers elected to serve through the Phoenix meeting are: president, Fred A. Henny; president-elect, Frank H. O'Halloran; vice-president, Lyall O. Bishop, and secretary-treasurer, Edward C. Thompson.

■ Illinois Announces Oral Surgery Courses Leading to M.S. Degree

The College of Dentistry of the University of Illinois is accepting applications for two and three year full time courses in oral surgery beginning in July 1960. Both programs carry credit toward a Master of Science degree.

Further information can be obtained from Daniel M. Laskin, department of oral and maxillofacial surgery, University of Illinois, 808 S. Wood St., Chicago 12.

■ Emory Dental School Offers Residency in Oral Surgery

In cooperation with the Emory University Schools of Dentistry and Medicine, approved two year residencies in oral surgery are available at the Atlanta Veterans Administration Hospital and Grady Memorial Hospital.

The residencies are approved by the Council on Dental Education of the American Dental Association and are recognized and accepted toward the partial fulfillment of American Board of Oral Surgery requirements.

Further information can be obtained from H. J. Harpole, professor of oral surgery, Emory University School of Dentistry, 106 Forrest Ave., N.E., Atlanta 3, Ga.

■ Oren A. Oliver to be Feted at Appreciation Banquet

An appreciation banquet honoring Oren A. Oliver of Nashville, Tenn., will be held Sunday, May 1, at the Hotel Peabody in Memphis. The Tennessee State Dental Association, during its ninety-third annual session, will be host. E. Jeff Justis, Trustee of the American Dental Association's Sixth District, is chairman.

■ Clinical Fellowships in Oral Pathology Offered at Pennsylvania

A clinical Fellowship in oral pathology, supported by the American Cancer Society, at the University of Pennsylvania, School of Dentistry, is open to qualified applicants. A tax-free stipend of $3,600 accompanies the Fellowship for one year beginning July 1, 1960.

Applications should include a curriculum vitae, academic record in dental school and at least two letters of reference. The deadline for receipt of all credentials is March 15. The address is: Committee on Fellowships and Traineeships, 4001 Spruce St., Philadelphia 4.

■ Oral Surgeons' Officer to Speak at Michigan Meeting

Edward C. Thompson of Urbana, Ill., secretary-treasurer of the American Society of Oral Surgeons, will be a featured essayist at the 103rd annual meeting of the Michigan State Dental Association May 2-4 at the Statler-Hilton Hotel, Detroit. Michigan has one of the largest state dental conventions in the nation, and more than 3,500 persons are expected to attend.

■ Hospital Dental Service Meetings Scheduled

The Council on Hospital Dental Service of the American Dental Association will meet April 11 and 12 at the Central Office of the Association in Chicago.

The Council also announces that it will be a co-sponsor of the Institute on Hospital Dental Service to be held jointly May 16-19 by the American Hospital Association and the American Medical Association. The institute will be held at the Henry Grady Hotel, Atlanta, Ga.

■ Eleventh Mid-Atlantic States Conference on Dentistry

The theme of the eleventh Mid-Atlantic States Conference on Dentistry is the "Contributions of the Basic Sciences to Current Clinical Practice." The conference, sponsored by the University of Pennsylvania School of Dentistry, will be held April 24-29 at the Hotel Hershey, Hershey, Pa.

Essayists will be Herbert K. Cooper, Stanley C. Harris, Ph.D., Wilton M. Krogman, Ph.D., John B. MacDonald, Balint J. Orban, George C. Paffenbarger and Harry Sicher, M.D.

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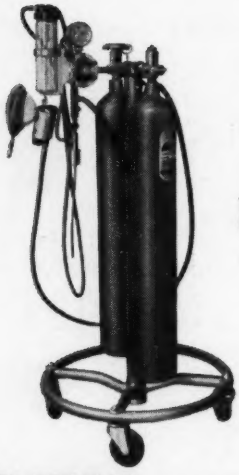

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